

June 2012

## NIEHS Spotlight



### [Birnbaum honored at AAAS and Heinz policy forums](#)

During May, two more organizations stepped forward to recognize NIEHS/ NTP Director Linda Birnbaum, Ph.D., for advancing the field of environmental health science.



### [Council ponders interesting times on the horizon](#)

As usual, there was a wide-ranging agenda at the 136th meeting of Council May 22-23 at NIEHS, including the current NIH budget situation.



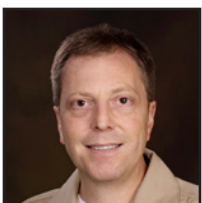
### [NIEHS Biomedical Career Fair attracts area trainees](#)

More than 350 participants gathered April 27 at the EPA main campus in RTP for the 15th Annual NIEHS Biomedical Career Fair.



### [Leadership develops data initiative](#)

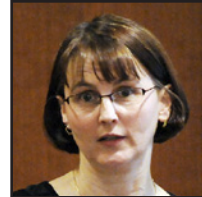
As toxicologists and other scientists accumulate exponentially greater volumes of information, they are faced with the challenge of managing the growing terabytes of data.



### [Shale gas workshop explores needed research on fracking](#)

NIEHS has taken a lead role in convening stakeholders, including the scientific and regulatory communities and industry, to help address questions about extraction.

## Science Notebook



### [Seminar addresses developmental origins of immune disease](#)

Biochemist Paige Lawrence, Ph.D., delivered a guest lecture April 26 at NIEHS on the relationship between environmental agents and defects in the immune system.



### [Cellular damage from normal metabolism potentially causes cancer](#)

New research from a team led by NIEHS scientists has identified DNA regions in yeast and in some cancers that have a disproportionately high number of mutations.



### [Researchers explore transgenerational effects of ancestral exposures](#)

The findings result from a productive collaboration between NIEHS-funded researchers at Washington State and U.S. Department of Defense scientists.



### [p53 may affect susceptibility to cancer and other diseases](#)

In her seminar, "Adventures in polymorphisms and p53 function," cancer biologist Maureen Murphy, Ph.D., discussed her research on variants in the p53 protein.

## NIEHS Spotlight



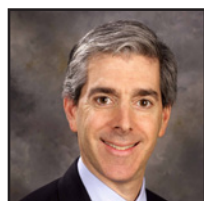
### [Breast cancer advocacy group honors NIEHS](#)

The Breast Cancer Fund celebrated its 20-year anniversary May 15 by honoring NIEHS and Director Linda Birnbaum, Ph.D., with its Heroes Award.



### [Institute celebrates third annual Ethics Day](#)

NIEHS celebrated the Institute's third annual Ethics Day May 9 with a program including two talks about ethical considerations at work and at the bench.



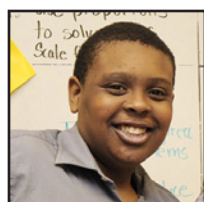
### [NIEHS gears up for Rio+20](#)

NIEHS sponsored or co-sponsored two events, during May, related to the upcoming Rio+20 United Nations Conference on Sustainable Development June 20-22.



### [Sandler honored by public health society](#)

NIEHS epidemiologist Dale Sandler, Ph.D., has been elected as an alumni member of the Johns Hopkins Chapter of the Delta Omega Honorary Society in Public Health.



### [Postdocs and apprentices wow middle school students](#)

The young apprentices showed off their new knowledge May 3 for parents, family, friends, and the community in a public showcase called WOW!



### [NIH Center for Regenerative Medicine launches website](#)

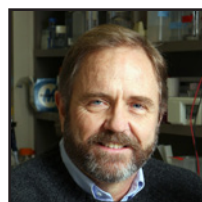
Scientists with an interest in the clinical translation of stem cell-based technologies now have an additional online resource with the launch of a new website.

## Science Notebook



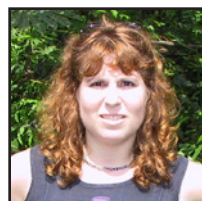
### [Genistein exposure linked to abnormal immune response and infertility](#)

New work from an NIEHS team of researchers suggests that changes to the immune system are partly responsible for genistein-induced rodent infertility.



### [Researchers pinpoint key protein that protects against septic shock](#)

The study is part of a larger, decades-long project that is exploring the differences in susceptibility to infection among individuals.



### [Genetic stature puzzle leads to interwoven complex traits](#)

New research with Pygmies suggests that variants leading to short stature could be attached to a genetic code beneficial for adapting to life in a tropical environment.



### [Cell Biology Group fellow wins travel award](#)

NIEHS visiting fellow Fumin Lin, Ph.D., used a \$1,000 travel award to attend the NIH Stem Cell Research Symposium May 10-11 in Bethesda, Md.



### [Council talks focus on DNA repair](#)

During their meeting May 22, Council members enjoyed scientific talks by award-winning researchers Leona Samson, Ph.D., and Thomas Kunkel, Ph.D.

## NIEHS Spotlight



### [Future NIH management leaders visit NIEHS](#)

A cadre of future NIH science management and policy leaders made the trek April 23 from Bethesda to North Carolina.



### [SRP graduate student receives prestigious fellowship](#)

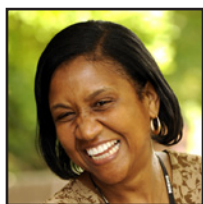
David Cipler, a graduate student in the Brown University Superfund Research Program, has received a prestigious Switzer Environmental Fellowship award.



### [WETP assembles DOE safety and health trainers](#)

More than 100 hazardous material and radiation safety and health trainers gathered May 7-8 in Knoxville, Tenn., to share best practices and new techniques.

## Inside the Institute



### [NIEHS health and fitness week becomes a family affair](#)

NIEHS marked this year's Health and Fitness Week, which began May 14, by including Family Day as part of the weeklong celebration.



### [Earth Day presentation on automotive technology](#)

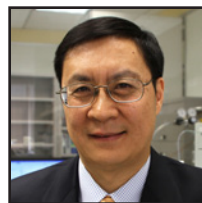
The NIEHS Environmental Awareness Advisory Committee hosted a presentation by automotive expert Richard Cregar May 3 as part of its Earth Day celebration.



### [Labs break for annual strawberry tradition](#)

NIEHS scientists in the Laboratories of Molecular Genetics and Structural Biology took a break from research to attend the 27th annual strawberry feast May 1.

## Science Notebook



### [Drastic reduction in air pollution may decrease CVD risk](#)

A new NIEHS-funded study led by Junfeng (Jim) Zhang, Ph.D., shows how air pollution contributes to cardiovascular disease risk.



### [CNS program participants gather at NIEHS](#)

The NIEHS Centers for Neurodegeneration Science (CNS) program held its fourth annual meeting May 3-4 at NIEHS.



### [Predicting breathing rates with personal exposure monitors](#)

A pilot study showed that new technology accurately predicted breathing rates for most of the 22 adult participants during a variety of activities.



### [Scientists explore developmental origins of disease](#)

Experts gathered May 14-16 to discuss the hypothesis that exposures during early development can lead to increased disease risk later in life.



### [This month in EHP](#)

This month's Environmental Health Perspectives features a discussion of some of the environmental health pros and cons of common packaging materials used for food.



### [Upcoming distinguished lecturer Rachel Green](#)

Rachel Green, Ph.D., will give a talk June 12 titled "Quality Control on the Ribosome During Translation," hosted by NIEHS lead researcher Traci Hall, Ph.D.



## Calendar of Upcoming Events

- **June 4**, in Building 101, F-193, 10:00-11:00 a.m. — Laboratory of Signal Transduction Seminar Series with Stephen Shears, Ph.D.
- **June 7-8**, in Rodbell Auditorium, June 7 – 8:30 a.m.-4:30 p.m., June 8 – 9:00 a.m.-12:30 p.m. — Seminar on “Environmental and Etiologic Implications of Parkinson’s Premotor Symptoms”
- **June 12**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Distinguished Lecture Series with Rachel Green, Ph.D., speaking on “Quality Control on the Ribosome During Translation”
- **June 14-15 (offsite event)**, at the National Academy of Sciences in Washington, D.C., June 14 – 8:30 a.m.-5:30 p.m., June 15 – 8:30 a.m.-12:00 p.m. — Emerging Science for Environmental Health Decisions Workshop on Systems Biology-Informed Risk Assessment, [Registration](#)
- **June 19**, in Building 101, F-193, 1:00-2:00 p.m. — Laboratory of Molecular Genetics Seminar Series with Jan Drake, Ph.D., speaking on “Like DNA replication, eukaryotic DNA mismatch repair is intrinsically asymmetric”
- **June 21-22**, in Rodbell Auditorium, June 21 – 8:30 a.m.-4:30 p.m., June 22 – 8:30 a.m.-12:00 p.m. — NTP Board of Scientific Counselors
- **June 23-26 (offsite event)**, in Houston, Texas — Endocrine Society Annual Meeting and Expo
- View More Events: [NIEHS Public Calendar](#)

## Science Notebook



### [Upcoming workshop on \*Leptospira\* vaccine potency testing](#)

The workshop will take place Sept. 19–21 at the USDA Center for Veterinary Biologics at the National Centers for Animal Health in Ames, Iowa.



### [Upcoming workshop on informed risk assessment](#)

An innovative interagency program continues its 2012 workshop series with an exploration of “Systems Biology — Informed Risk Assessment” June 14-15.

## Extramural Research

### [Extramural papers of the month](#)

- [Prenatal exposure to PAHs linked to childhood obesity](#)
- [BPA associated with IVF implantation failure](#)
- [Guidelines for risk of illness from beach sand](#)
- [DNA mismatch repair introduces mutations in non-dividing cells](#)

## Intramural Research

### [Intramural papers of the month](#)

- [Chromatin structure changes during course of glucocorticoid receptor activation](#)
- [Novel assay measures DNA breaks in human cells exposed to tumor inhibitors](#)
- [Mechanism for endocrine disrupting chemicals is dose and cell type specific](#)
- [SIRT1 is a crucial regulator of mammalian metabolic homeostasis](#)



## Birnbaum honored at AAAS and Heinz policy forums

By Eddy Ball

During May, two more organizations stepped forward to recognize NIEHS/NTP Director Linda Birnbaum, Ph.D., for advancing the field of environmental health science. Birnbaum gave high profile, potentially high-impact presentations before audiences involved in scientific policy related to the environment and public health, at the American Association for the Advancement of Science (AAAS) auditorium in Washington, D.C.

Birnbaum was one of three speakers May 8 at the Heinz Center's third [Horizons@Heinz](#) environmental policy lecture, joining colleagues and NIEHS grantee [Thomas Zoeller, Ph.D.](#), and Environmental Health News communications fellow [Laura Vandenberg, Ph.D.](#), addressing the impacts of low doses of endocrine disruptors on human and ecosystem health. The organization describes the speakers in its series as environmental visionaries. Previous speakers have offered insight into the economic value of natural resource preservation and the emerging field of green chemistry.

Following her nomination by NIEHS lead researcher Traci Hall, Ph.D., AAAS selected Birnbaum to deliver the [Robert C. Barnard Environmental Lecture](#) May 24, as part of the 2011-2012 AAAS Science and Technology Policy Fellowships program. She spoke to a target audience of current class fellows, former fellows from the D.C. area, regional policymakers, and scientists, as well as representatives of nongovernmental organizations, think tanks, businesses, universities, and other entities with a focus on environmental issues.

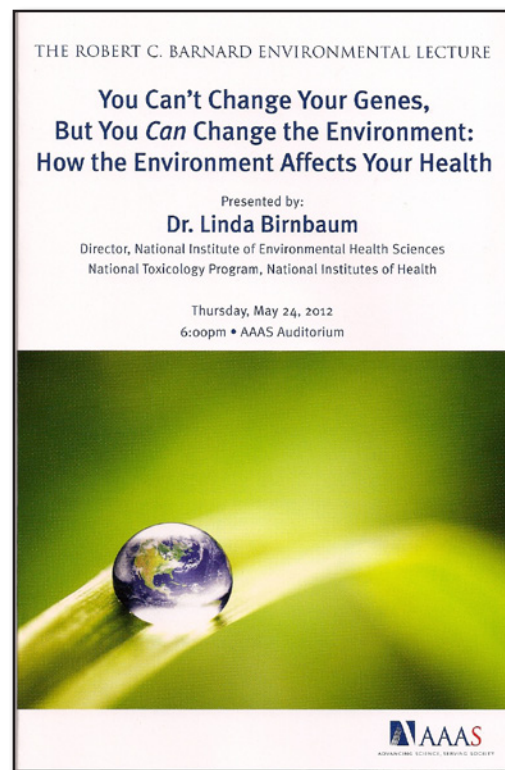
### Redefining what dosages matter in endocrine disruption

As the third speaker on the Horizons@Heinz program, Birnbaum introduced her talk with an overview of endocrine disruption and the rise in diseases linked to hormonal effects from the environment on every organ of the body. She then gave her audience a clear statement of what to expect in her presentation.

"I'd like to emphasize four main points about endocrine disruptors today," she said. "First, low doses can have big effects. Second, endocrine disruptors can have a wide range of effects on our health. Third, early life exposures can have persistent effects. And, fourth, endocrine disrupting chemicals are ubiquitous."



*Birnbaum is both the first head of a federal agency and the first woman to present a Robert C. Barnard Environmental Lecture. (Photo courtesy of Steve McCaw)*



An important part of Birnbaum's discussion was the concept of developmental origins of disease. She explained that endocrine disruption during critical windows of susceptibility, during gestation and development, as well as into middle and later life, can trigger disease processes that may not manifest until decades after the initial exposure.

"Often, endocrine disruptors are present at biologically effective levels, and exposure to humans is common," she explained, making their effects on human health a significant public health policy issue.

### **Engaging science and public health policy toward primary prevention**

During her Barnard lecture, "You can't change your genes, but you can change your environment: How the environment affects your health," Birnbaum developed a theme that runs through many of her public talks — the importance of environmental health research supported by NIEHS and NTP in making informed policy decisions to shape primary prevention strategies.

Birnbaum began with the basics — the dramatic increase in diseases, such as testicular cancer and breast cancer, growing evidence of the environmental role in disease etiology and progression, and the expanded definition of the environment. She then moved into the concepts of low-dose toxicology, the developmental origins of disease, and the role of epigenetics in setting the stage for the development of disease.

## **An essential message for policymakers now and in the years to come**

Near the end of her Barnard lecture, Birnbaum summarized her wide-ranging presentation for the audience of influential policymakers. "Our environment is one of the most important determinants of our health and our quality of life," she told the attendees.

"Our Institute, the NIEHS, is united by a desire to understand and prevent environmental influences on disease. This is one of the most ambitious missions of all the institutes of the NIH, embracing all parts of the body and all diseases with environmental aspects, which we are learning means virtually all diseases, since even many diseases with genetic causes also have environmental components or triggers."

### **Influential forums for public health policy**

- The Horizons@Heinz lecture series is one of many programs funded by the non-profit H. John Heinz III Center for Science, Economics, and the Environment. The Center's initiatives promote responsible ecosystem management, biodiversity, environmental quality, and enhanced environmental public health. Its projects address environmental issues worldwide, from the Navajo lands in the Southwestern U.S., to South Africa, the Arctic, and the Amazon.

The center's mission parallels efforts supported by the Heinz Family Philanthropies, chaired by Teresa Heinz, widow of Sen. John Heinz and vice chair of the Heinz Center. The organization funds annual awards, endowed professorships, and scholarships, in addition to other programs.

- Since its inception in 1999, the Robert C. Barnard Environmental Lecture has provided a forum for distinguished speakers from a wide range of fields to address current environmental issues. The series honors [Barnard](#), a prominent attorney who died in 2003, for his contributions to environmental and public health law, and in recognition of his many years of service as a member of the selection committee for the AAAS fellowships at the U.S. Environmental Protection Agency.

Endowed by the international law firm of Cleary, Gottlieb, Steen, and Hamilton LLP, where Barnard was counsel, the series perpetuates his commitment to bringing good science to bear on government decision making.

After reporting on research linking obesity and diabetes, at least in part, to environmental exposure, Birnbaum made the case for testing the tens of thousands of unregulated chemicals in the environment, using the Tox 21 program of predictive toxicology high-throughput screening and bioinformatics to help clear the backlog. Birnbaum worked up to her resounding conclusion ([see text box](#)) by looking forward to emerging health issues, such as nanomaterials and hydraulic fracturing; ongoing disaster response programs, most notably the GuLF STUDY; and the Institute's newly crafted five-year strategic plan.

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## Council ponders interesting times on the horizon

*By Ernie Hood*

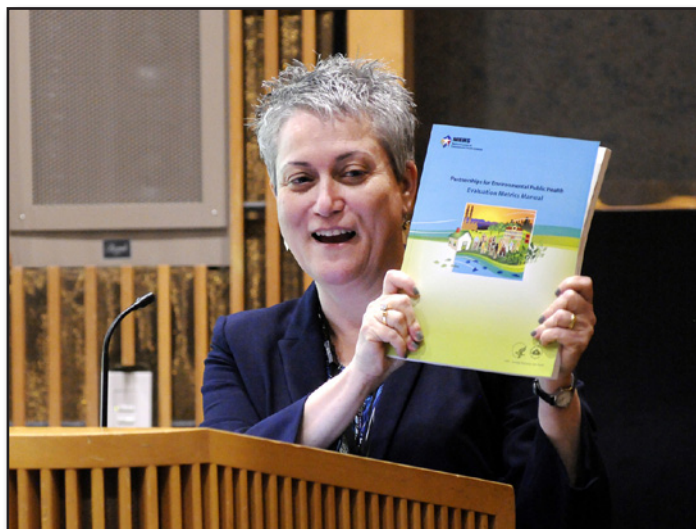
As usual, there was a wide-ranging agenda at the 136th meeting of the National Advisory Environmental Health Sciences Council May 22-23 at NIEHS, including the current NIH budget situation. Like its sister institutes and centers, NIEHS could be facing what one speaker described as interesting times and challenging times in the year ahead, at a time when the environmental health sciences are achieving major advances in research and the application review process.

### Strategic plan nearing the finish line

NIEHS/NTP Director Linda Birnbaum, Ph.D., updated Council on a variety of news and highlights from the institute since its last meeting in February, including recent meetings and events, awards, and scientific publications. She reported that the new NIEHS strategic plan for 2012-2017 is nearing completion. The [current draft](#), which includes eleven strategic goals, was posted to the NIEHS website in April.

“What we’re working on right now is developing implementation strategies,” Birnbaum told the Council members. “These are the internal strategies that NIEHS is developing to define what we will do, when we will do it, and how much it will cost.” The finalized plan is scheduled to be published in July, following an intensive 18-month process spearheaded by NIEHS Deputy Director Richard Woychik, Ph.D.

Birnbaum noted that there is no expectation that Congress will enact a budget prior to the fall election, and may not do so until after the new president and Congress are seated in January, meaning funding will continue at current or reduced levels until such time as a budget is passed.



*Collman distributed hard copies of the new Partnership for Environmental Public Health [Evaluation Metrics Manual](#), which is also available electronically on the NIEHS website. (Photo courtesy of Steve McCaw)*



*Birnbaum addressed the progress of the new NIEHS strategic plan and updated Council on a broad range of other topics. (Photo courtesy of Steve McCaw)*



Although other agencies within the U.S. Department of Health and Human Services and other parts of the government have already seen or are bracing for substantial budget cuts, she said the outlook for NIEHS is a flat budget, which is, actually, a positive outcome given the current atmosphere. Birnbaum announced, per a recent executive order, that a 30 percent cut in travel expenses is to be implemented, along with preapproval and additional reporting and record keeping associated with conference expenses.

## On the extramural front

Division of Extramural Research and Training (DERT) Director Gwen Collman, Ph.D., reported that there continues to be good progress in improving the review process for environmental health sciences applications at the NIH Center for Scientific Review. The Systemic Injury from Environmental Exposure Special Emphasis Panel (SEP) will be reconstituted, running as a trial for 2-3 review cycles, and possibly going on longer, if needed. The first meeting of the reconstituted SEP is anticipated to be held in February 2013, for review of applications submitted this fall. “The idea over the long term is to establish a chartered study section with permanent membership to incorporate the needs of our field,” Collman noted.

She also briefed Council on a possible new NIH policy for fiscal year 2013, mandating a process for special Council review of funding applications from investigators with more than \$1.5 million in total research costs. She outlined the criteria for inclusion and how the threshold would be determined.

## Interesting times, challenging times

That was the message from Sally Rockey, Ph.D., deputy director for extramural research at NIH, as she described the many options being weighed in Bethesda, Md., for [how to manage flat or dwindling research funding in austere times](#).

She noted that the NIH budget is flat under the [President’s FY2013 budget proposal](#) but, echoing Birnbaum’s assessment for NIEHS, she said, “Considering the tough economic times that all of the federal government is under, having a flat budget proposal from the President actually was a win for us.” At the same time, NIH is being asked to keep the number of new and competing research project grants steady or even to increase them. With a flat budget, she explained, keeping flat or increasing competing awards puts pressure on all of the organization’s past commitments.

One option for NIH is to continue to manage NIH resources much as in the past, but to simply trim spending across the board. That would involve no systemic changes, only annual belt-tightening for all programs, which could result in continued reductions in success rates in grant applications, and could risk innovation as applicants play it safe to get through peer review.

Other options being pondered include reducing or limiting the average size of an award, limiting the number of awards held by a grantee, limiting the amount of funds a grantee can hold, or even limiting salaries of grantees.

Each of those options has its advantages and disadvantages, but according to Rockey, the only one that would result in significant savings would be limiting the amount of funds a grantee could hold. The major objection to that redistributive approach, said Rockey, is that NIH is essentially a meritocracy. “That’s what we’re about,” she said. “We believe that the best science should be funded regardless of who’s doing it, so this would be quite a different mindset for how we support science in this country.”

For more information and her thoughts on managing NIH resources in austere times, follow Rockey’s NIH Office of Extramural Research blog, [Rock Talk](#).

## Program concepts get the green light

Fred Tyson, Ph.D., of the DERT Cellular, Organ, and Systems Pathobiology Branch, detailed a program called Toxicant Exposures and Responses by Genomic and Epigenomic Regulators of Transcription (TaRGET), a four-phase initiative designed to accelerate progress in epigenetics and epigenomics using the latest sequencing technology and integrating environmental exposure data from population studies.

Following up on the results of an [expert panel workshop](#) held in 2010, Health Scientist Administrator Michael Humble, Ph.D., presented a proposed Funding Opportunity Announcement titled “Role of the Environment in the Development of Autoimmune Disease.” The \$2.5 million program would support 6-8 awards for innovative basic, epidemiological, and interdisciplinary research aimed at understanding mechanisms by which the environment and environmental exposures influence the development and exacerbation of autoimmune disease.

Council also enjoyed two scientific presentations ([see related story](#)), an overview of the NIH budget process, an analysis of the progression of the NIEHS neurodegeneration research portfolio from 1986-2009, and a candid report from the NIH Deputy Director for Extramural Research, Sally Rockey, Ph.D. ([see text box](#)).

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison.)



NIEHS leadership met with Council for the second time this year May 22-23 in Rodbell Auditorium at NIEHS. Show left to right are DERT Deputy Director Pat Mastin, Ph.D., Collman, Birnbaum, NIEHS Scientific Director Darryl Zeldin, M.D., and Woychik. (Photo courtesy of Steve McCaw)



Council members Marie-Francoise Chesselet, M.D., Ph.D., left, and Thomas Gasiewicz, Ph.D., paid close attention to the presentations during the meeting. (Photo courtesy of Steve McCaw)



Council member Edward Postlethwait, Ph.D., was one of several advisors with comments and questions for presenters. (Photo courtesy of Steve McCaw)



In addition to her discussion of NIH budget management efforts, Rockey briefed Council on the [findings](#) of the NIH Working Group to Examine the Future Biomedical Workforce. (Photo courtesy of NIH)

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# NIEHS Biomedical Career Fair attracts area trainees

*By Darshini Trivedi*

More than 350 participants gathered April 27 at the U.S. Environmental Protection Agency (EPA) main campus in Research Triangle Park, N.C., for the 15th Annual NIEHS Biomedical Career Fair.

The Biomedical Career Fair has been part of a long-standing tradition at NIEHS, and is focused on providing young scientists with an opportunity to explore a myriad of job choices and expand their professional networks. As in previous years, this event was organized by postdoctoral fellows from the [NIEHS Trainees Assembly \(NTA\)](#) and the EPA, with support from the NIEHS Office of the Scientific Director.

The event began with opening remarks from William Schrader, Ph.D., NIEHS deputy scientific director, and David Thomas, Ph.D., of the EPA National Health and Environmental Effects Research Laboratory. A highlight of the career fair was a keynote address from Adam Ruben, Ph.D., a scientist at Sanaria Inc. and author of the book, “Surviving Your Stupid, Stupid Decision to Go to Grad School.” Ruben delivered a comedy-filled presentation by drawing from some of his own experiences as a graduate student, while also giving hope to aspiring scientists by talking about his current successful job in the real world.

## A positive and encouraging message for young, aspiring scientists

The overall goal of this year’s career fair was to showcase Ph.D. scientists who have transitioned into a career within the last two to three years. “We want to emphasize to our attendees that, yes, you can still be successful in obtaining a job in this current economic situation,” said Ashley Godfrey, Ph.D., co-chair for the planning committee and an NIEHS postdoc. Former NIEHS postdocs ([see text box](#)), who have recently moved on to achieve successful positions in a variety of career tracks, traditional as well as non-traditional, were one of the main highlights of this year’s event. When asked about her overall impressions of the career fair, NIEHS postdoc Kymberly Gowdy, Ph.D., said, “This is the best career fair I have been to so far!”

The program for the day was packed with several panel discussions showcasing a variety of careers, as well as career development workshops designed to help the attendees develop the skills and obtain the necessary tools for a successful job. The planning committee was thrilled to invite back Diane Klotz, Ph.D., former director of the [NIEHS Office of Fellows’ Career Development](#), who departed last year to accept the position of director



*Ruben turned the title of his book upside down, as he talked about how his education and his experiences as a graduate student led to a multifaceted career as author, humorist, and scientist. (Photo courtesy of Steve McCaw)*



*A packed room of young scientists enjoyed the comedy-filled keynote address. (Photo courtesy of Steve McCaw)*



of the Office of Training and Academic Services at Sanford-Burnham Medical Research Institute. Klotz, a career development expert who was monumental in the planning of the previous career fairs, presented two workshops titled “Finding your Career Path” and “The Industry Job Search — Navigating Towards Your Next Opportunity.”

The planning committee brought back the popular one-on-one curriculum vitae/resume consultation sessions by career experts, and also hosted a networking lunch and afternoon reception to provide the participants an opportunity to meet informally with panelists, workshop leaders, other career fair attendees, and many exhibitors from local and regional companies and organizations.



*Klotz, who completed her postdoc at NIEHS, talked to the audience about taking control of their own career paths. (Photo courtesy of Steve McCaw)*



*Sunman discussed his career transition from the bench to patenting, one that involved extracurricular training in patent law and networking at the Biomedical Career Fair. (Photo courtesy of Steve McCaw)*

## Career Fair showcases former NIEHS trainees

Hearing about how other fellows made the transition from training to careers is an important part of career development programs. But for NIEHS fellows, this year’s Biomedical Career Fair was even more meaningful, because so many panelists were former colleagues at NIEHS, including members of the following panels:

- Careers in Teaching-Intensive Schools — Shweta Trivedi, Ph.D., teaching assistant professor at North Carolina State University
- Project/Program Management — Thaddeus Schug, Ph.D., a health scientist in the NIEHS Division of Extramural Research and Training
- Science Outreach — Jana Stone, Ph.D., scientific coordinator at the Duke University Center for Systems Biology
- Careers in Research-Intensive Schools — Chris Geyer, Ph.D., assistant professor at East Carolina University
- Science Communications — Heather King, Ph.D., senior science communications specialist with MDB, Inc.
- The Business of Science — Jeff Sunman, Ph.D., patent agent with Alston and Bird LLP
- Field Applications — Andres Larrea, Ph.D., field applications scientist with Pacific Biosciences
- Careers in Small Biotech — Kelly Mercier, Ph.D., applications scientist with LipoScience, and Patrick Robertson, Ph.D., scientist II with Fujifilm Diosynth Biotechnologies
- Clinical Research — Joan Packenham, Ph.D., director of the NIEHS Office of Human Research Compliance





*NIEHS fellows Tracy Clement, Ph.D., left, and Katie Burns, Ph.D., right, took advantage of the networking session to get more one-on-one career advice from Marsha Cole, Ph.D., a Careers in Research-Intensive Schools panelist. (Photo courtesy of Steve McCaw)*



*Larrea networked with a trainee, while offering useful career advice as attendees visited exhibits. (Photo courtesy of Steve McCaw)*



*The 2012 NIEHS Biomedical Career Fair Planning Committee comprised of fellows from NIEHS and EPA. Shown left to right, back row: Christy Powers, Ph.D. (EPA); Stela Palii, Ph.D.; Shep Martin, Ph.D. (EPA); Brant Hamel, Ph.D.; Staton Wade, Ph.D.; and co-chair Ashley Godfrey, Ph.D. Shown left to right, front row: Sabrina Robertson, Ph.D.; Bhargavi Rao, Ph.D.; Maria Shatz, Ph.D.; co-chair Darshini Trivedi, Ph.D.; and Cynthia Holley, Ph.D. Not shown in picture: Teresa Green, Ph.D. (EPA) and Rachel Goldsmith, Ph.D. (Photo courtesy of Steve McCaw)*

(Darshini Trivedi, Ph.D., is an Intramural Research and Training Award fellow in the NIEHS Laboratory of Toxicology and Pharmacology.)



# Leadership develops data initiative

By Eddy Ball

As toxicologists and other scientists accumulate exponentially greater volumes of information, they are faced with the challenge of managing the growing terabytes of data.

In a talk May 8 at the U.S. Environmental Protection Agency (EPA), NIEHS/NTP Director Linda Birnbaum, Ph.D., shared the Institute's strategy for moving NIEHS towards a more collaborative approach to science and the infrastructure required to enhance discovery with its new e-Science Data Coordination initiative. Birnbaum and representatives of other agencies spoke during the federal perspective segment of [Building for Better Decisions: Multi-Scale Integration of Human Health and Environmental Data](#), organized and primarily sponsored by the Society of Toxicology.

Joining Birnbaum in the federal perspective segment were representatives of data integration efforts underway at the EPA, U.S. Food and Drug Administration, U.S. Geological Survey, U.S. Nuclear Regulatory Commission, U.S. Department of Defense, and U.S. Department of Agriculture.

## Supporting big science in a time of limited resources

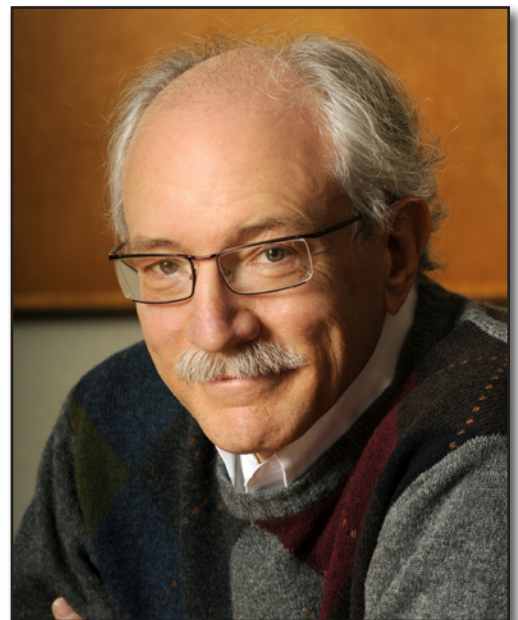
As Birnbaum explained, NIEHS and NTP have major interests in maximizing the Institute's substantial investment in research, by promoting secondary data analyses, merging existing data resources, and coordinating efforts by research groups to address common and prevalent diseases. Environmental data coordination offers an efficient and cost-effective strategy for accelerating the translation of new and existing information about genetic and environmental interactions into clinical and public health practice.

Federal agencies also need to meet new challenges posed by the evolution of science, as more and more large-scale, multi-author studies generate enormous amounts of data that can strain existing data management infrastructure.

"The small-science approach to management and sharing of digital biomedical research data is anachronistic," Birnbaum told her audience. "It's at variance with the growing emphasis, both in U.S. policy and around the world, on open access to scientific data, and it may put the results of important research investments at risk and impede long-term access to valuable scientific resources."



*"As the Institute embarks on crafting a new strategic plan and redefining future directions," Birnbaum explained, "science and services supporting the information and research needs of the Institute must evolve as well." (Photo courtesy of Steve McCaw)*



*Woychik, above, and Dearry will build an infrastructure for the initiative with resources in the NIEHS Office of the Deputy Director and Library and Information Services Branch. Birnbaum said there would be fundamental changes in current data management and dissemination practices. (Photo courtesy of Rick Woychik)*



## Integrating databases is the foundation for a new data integration paradigm

Birnbaum pointed to the success of ongoing efforts to expand the NIEHS Chemical Effects in Biological Systems (CEBS) database that includes studies of the biological context of response to chemicals, environmental agents, genetic changes, and physical agents. From its inception in 2005, the library accessible through CEBS has grown from 12 to more than 9200 articles, with plans to integrate even more NTP and public sources over the next year, including the DrugMatrix® database, one of the world's largest toxicogenomics reference resources ever assembled, acquired in 2011.

Digital technology can make data openly accessible to scientists, reducing data management burdens, formalizing generalizable and replicable science, and enabling new kinds of data-driven science. As Birnbaum reminded attendees, a comprehensive plan must also address the complex managerial and ethical considerations of data integration, which include at least the following three elements:

- Data management and sharing standards for the entire lifecycle of various kinds of digital data.
- Compliance of researchers with relevant internal and external standards and requirements.
- Criteria for deciding the appropriate level of management and preservation.

Birnbaum has selected NIEHS Deputy Director Rick Woychik, Ph.D., and Special Advisor Allen Dearry, Ph.D., to serve as leads on the new e-Science Data Coordination initiative.



*Dearry is the NIEHS liaison for the U.S. Department of Health and Human Services Health Data Initiative. (Photo courtesy of Steve McCaw)*

### Recent stories about data management, sharing, and integration

- [Workshop seeks to expand and improve data sharing](#) — Nearly 100 environmental health researchers, NIEHS program administrators, and other interested government officials gathered Feb. 6-7 in Research Triangle Park, N.C.
- [Presidential advisor discusses Health Data Initiative](#) — U.S. Department of Health and Human Services Chief Technology Officer Todd Park gave a spirited talk April 5 at NIEHS about the Health Data Initiative.
- [GEMS goes transdisciplinary with spring meeting](#) — The agenda was designed to highlight emerging environmental issues, including the need to develop comprehensive data management strategies.

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# Shale gas workshop explores needed research on fracking

By Cindy Loose

As the world struggles to meet its growing need for energy by exploring new fuel sources and extraction methods, NIEHS wants important public health questions asked and answered.



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For example, chemicals are being pumped deep into the earth to release natural gas in thousands of wells using the new technology known as hydraulic fracturing, or hydrofracking. Does hydrofracking also mobilize naturally occurring hazardous compounds?

NIEHS has taken a lead role in convening stakeholders, including the scientific and regulatory communities and industry, to discuss and help address these questions. Most recently, the NIEHS-sponsored Institute of Medicine Roundtable on Environmental Health Sciences, Research, and Medicine hosted a [workshop](#) April 30-May 1 in Washington, D.C., that brought together scientists, industry, and government.

The attendees explored what potential environmental threats, both above and below ground, may be posed by hydrofracking. An important part of the discussion was the consideration of who will be responsible for studying the various aspects of the complex, but straightforward, question, “What are the short- and long-term impacts of hydrofracking on human health?”



*Miller is the lead for the NIEHS and NTP response to fracking. (Photo courtesy of Steve McCaw)*

## Balancing risks and benefits of a new energy source

The nation’s need to reduce greenhouse gas emissions, and desire to decrease dependence on foreign energy, have helped spur development of gas wells using new technology that extracts methane, at depths of up to 7,000 feet, from natural shale deposits. At the workshop, a Shell representative explained the process by which directional drilling is combined with millions of gallons of water, plus various additives, to release the gas. Substances used in the process include acids, gelling agents, biocides, anti-corrosives, and friction reducers. Enormous quantities of sand are also needed to keep fracture channels open.

As IOM reported after the [workshop](#), “Public health was not brought into discussions about shale gas extraction at earlier stages; in consequence, the health system finds itself lacking critical information about environmental health impacts.”

“At this stage, the federal agencies are still developing strategies for examining the myriad of issues involved,” said NIEHS Senior Advisor John Balbus, M.D. “Efforts like the recent workshop inform those discussions.”

Balbus represented NIEHS on a workshop panel that also included senior leadership from the U.S. Geological Survey, the Occupational Safety and Health Administration, and the Centers for Disease Control and Prevention (CDC).

Panel members addressed, among other issues, what they saw as their agencies’ roles for action; how local, state, and federal institutions should coordinate efforts; and what other partners should be engaged.

“The workshop and other engagements by NIEHS are critical in playing a catalytic role in informing the agenda not only for NIEHS, but for all stakeholders,” said NIEHS Senior Medical Advisor Aubrey Miller, M.D., who is coordinating the NIEHS response to hydrofracking.

### NIEHS and NTP initiatives

NIEHS recently issued a [request for proposals](#) from the research community that, for the first time, includes language specific to hydrofracking among other topics. “Interest in the health issues around hydrofracking has been picking up intensity both among scientists and the general public,” said Miller.

Part of the NIEHS effort involves activating and coordinating the work of its [Environmental Health Sciences Core Centers](#) around the nation. Research interests expressed by the centers include gathering base line data in communities, studying components of fracking chemicals, and epidemiological studies that investigate health trends where the number of these wells is growing exponentially.

The centers have recommended developing a map to show locations of both wells and experts, and they plan to strengthen partnerships with the CDC, the U.S. Environmental Protection Agency, and professional groups.

Additionally, NTP has begun examining the needed research about toxicological issues. Among questions identified as needing further investigation were “Are known hazardous compounds, at levels of concern, contaminating groundwater and ambient air?” and “What is the composition and environmental fate of flowback water?”

Of particular interest is understanding the toxic effects of both intense short-term and chronic low-level exposures of hydrogen sulfide (H<sub>2</sub>S). Although high levels of H<sub>2</sub>S exposure are known to cause severe neurologic and respiratory symptoms, loss of consciousness, and even death, much less is known about chronic low-level exposures. NTP has also identified a need for investigation into what additional chemicals should be monitored in the air in communities near hydrofracking operations.

(Cindy Loose is a contract writer with the NIEHS office in Bethesda, Md.)

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## Breast cancer advocacy group honors NIEHS

*By Ed Kang*

The Breast Cancer Fund (BCF), a California-based breast cancer advocacy organization, celebrated its 20th anniversary May 15, by honoring NIEHS and Director Linda Birnbaum, Ph.D., with its [Heroes Award](#). The annual distinction recognizes groundbreaking research and dedication towards eliminating the environmental causes of breast cancer. A gala event at the Yerba Buena Center for the Arts in San Francisco spotlighted the contributions of the Institute and more than 50 prior Heroes Award recipients, many of whom were in attendance.



*Balbus represented NIEHS at the IOM workshop. (Photo courtesy of Steve McCaw)*



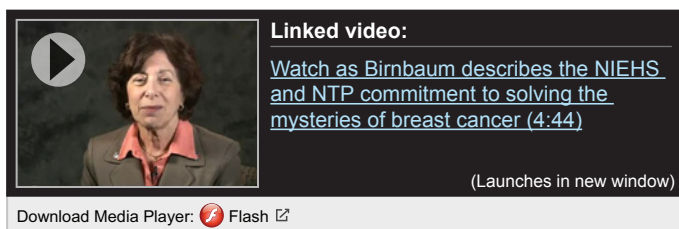
BCF Chief Executive Officer Jeanne Rizzo, who is also an appointed member of the National Institutes of Health Interagency Breast Cancer and Environment Research Coordinating Committee and a member of the NIEHS Public Interest Partners, emceed the event. In announcing NIEHS as the 2012 Science Hero awardee, she said, “NIEHS and NTP are key to our understanding of the role of environmental exposures in breast cancer risk. The Breast Cancer Fund heralds NIEHS’s contributions, which will ultimately prevent many breast cancers.”

### A partnership of scientists and advocates

Birnbaum was not available to receive the award in person but, in her videotaped remarks, she accepted the Breast Cancer Fund award by saying, “Solving the mysteries of breast cancer has been a research priority for us and, for that, I’m extremely proud to be representing NIEHS.” She further committed to continue the relationship with advocates and communities to prevent breast cancer from environmental contributors.



*Collman, left, joined Rizzo at the Heroes Award celebration. In receiving the award on behalf of the Institute, Collman recounted the long relationship that began with former NIEHS Director Ken Olden, Ph.D., and BCF founder Andrea Martin. (Photo courtesy of Bennett Sell-Kline)*



In Birnbaum’s absence, Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, was on hand to thank the audience of more than 550 attendees, and to highlight the relationship between NIEHS and the Breast Cancer Fund, which has grown more deeply over time. “Over the years, our organizations have found many ways to advise each other and to look for opportunities for collaboration, as the advocacy community has become more integrated in the development, implementation, and dissemination of scientific research.”

She also referred to the strong relationships and mutual appreciation for each other’s work as a paradigm to be emulated. “I think the advocates see the advantages of learning about the science,” Collman remarked. “And our scientists can learn about what it means to be a survivor and how important it is to get a diversity of voices around the table.”

Collman concluded by thanking the advocacy community for their immeasurable contributions to the research process, and mirrored Birnbaum’s sentiments by highlighting the commitment to work together as a community to more fully understand the causes of breast cancer.



*In her videotaped remarks, Birnbaum acknowledged the many people behind the scenes working on breast cancer-related research. She said, “Our dedicated staff and thousands of grantees do a tremendous job every day to make our lives, our homes, and our communities healthier and safer.” (Photo courtesy of Steve McCaw)*

Prior winners of the Breast Cancer Fund Heroes Award include philanthropist Teresa Heinz, Senator Tom Harkin (D-Iowa), Congresswoman Nancy Pelosi (D-Calif.), actor Jill Eikenberry, and dozens of other notable advocates, scientists, and politicians.

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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## Institute celebrates third annual Ethics Day

*By Melissa Kerr*

NIEHS celebrated the Institute's third annual Ethics Day May 9 with a program including two talks about ethical considerations at work and at the bench. Participants also enjoyed a break between the talks, with good-natured competition and laughter, during a mock game show titled "Who Wants to Be an Ethics Millionaire" ([see text box](#)). Hosted by NIEHS [Office of Ethics](#) Director and Deputy Ethics Counselor [Bruce Androphy, J.D.](#), the theme of this year's program was "We're Here to Help!"

Co-hosted by NIEHS/NTP Director Linda Birnbaum, Ph.D., the program was filled with games, songs, and presentations. She said the program was designed to promote discussion and to help avoid pitfalls that can lead to ethics violations. She stressed that people should always ask first, and never act on assumptions, if a situation seems in any way questionable. After Androphy introduced the staff of the Office of Ethics, he explained why ethics is important. "Innocent behavior can easily violate regulations and policies," he said.

### Value judgments in scientific research

The first speaker on the program was [Kevin Elliott, Ph.D.](#), from the philosophy department at the University of South Carolina. His presentation, "Ethics and Value Judgments in the Environmental Health Sciences," focused on how ethical decisions impact scientific objectivity. His discussion detailed how seemingly straightforward decisions, such as which endpoints to examine or even what kind of wording to use, can make a difference in how scientific research is viewed.

Author of a book on the topic, Elliott outlined three basic options to help a scientist make a value judgment. First, a scientist can try to establish personal boundaries in regard to ethical judgments. Second, a scientist can strive to focus solely on the science and allow policymakers to make the judgment calls. The final option is to use a balanced approach when making these decisions.

None of the options are free from drawbacks. "These aren't easy issues," he stressed.



*Androphy joined Birnbaum onstage, at the beginning of the event, in a song about filing ethics reports, outside activities, and financial disclosure called "Let My People File." Like the rest of the program, it combined a serious message about ethics with levity. (Photo courtesy of Steve McCaw)*



Elliott said he believes that scientists can justify making judgment decisions based on the range of society's priorities. "Perhaps you folks have a special role to play as government scientists in dealing with these value judgments in ways that serve the public interest," he said in closing.

### **Ethics in personal lives, communities, and the workplace**

The final part of the ethics program was dedicated to applications of ethical decisions in several areas, including environmental law. Meave Tooher, J.D., who once worked with Androphy, is currently with Tooher & Barone, LLP, a law firm in New York specializing in environmental law and ethics. In her talk, "Tales from the trenches – real life ethics adventure," she drew upon the current controversy over proposed hydraulic fracturing in Western New York, as well as a number of examples from her work with the New York State Ethics Commission.

"Ethics is real life," she said. "Ethical choices all flow from who you are."

Tooher reinforced the message that people should ask first. "If it confuses you at all," she told the audience, "ask someone." She pointed to many situations in which a simple question could have saved reputations and even jobs. It is much harder to defend a questionable decision after being accused of unethical behavior, she explained, especially if the case becomes high profile and attracts media coverage.

She also discussed pressures created by society's insatiable desire to know. There is a difference, she explained, in transparency and being under the microscope. The way for scientists and others to lessen the pressure in making judgment calls is to become more informed about how others see a situation and better anticipate issues that could arise.

During the question and answer session following Tooher's talk, Birnbaum discussed the need for transparency, and how looking at science from that standpoint may make ethics decisions a bit easier to manage. She hopes that before scientists make a decision, they try to look at what they are doing and saying in a neutral fashion. "Try to lay out what your assumptions are and what your guidance is," she said.



*Elliott smiled, as NIEHS Bioethicist David Resnik, J.D., Ph.D., introduced him to the audience. Elliott used familiar examples from NIEHS and RTI International researchers, as he discussed the way value judgments can inform scientific discourse. (Photo courtesy of Steve McCaw)*

### **And now for a little comic relief — becoming an ethics millionaire**

The money was make believe, and there was never much doubt that Birnbaum would receive the winning check, but the fun-filled game, sandwiched between the very serious talks, helped drive home the importance of ethics at NIH and NIEHS. Birnbaum and her panel of advisers answered a series of 15 increasingly difficult questions about ethics at NIEHS, at times engaging the audience to vote for the correct answer.

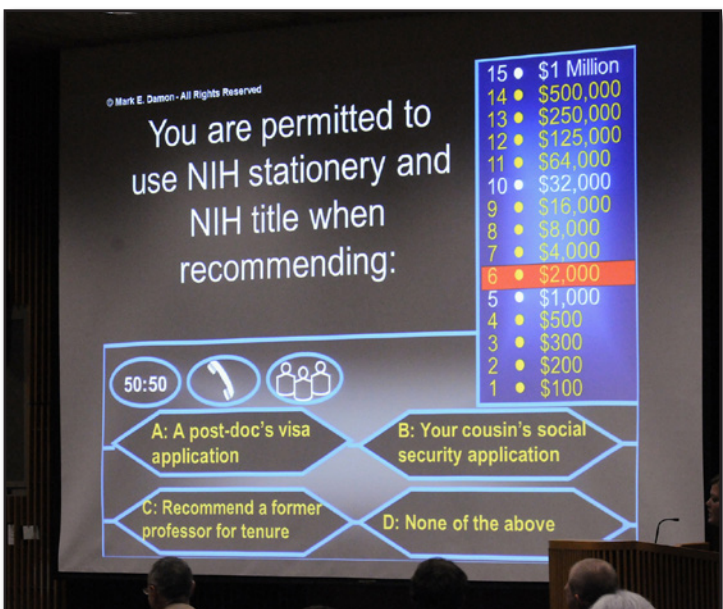
Androphy and his staff managed to communicate several important messages about ethics. The permitted action isn't always the one that simply feels right; the rules are not always intuitive, and they may be interpreted differently by different government agencies; and, it's always better to ask first, rather than be forced to defend a decision afterwards.



Student Temporary Employment Program staffer Casey Bledsoe emceed the mock game show. Like everyone else involved, she seemed to thoroughly enjoy the experience. (Photo courtesy of Steve McCaw)



In the end, Birnbaum took home the top prize. (Photo courtesy of Steve McCaw)



As the stakes became higher, the questions grew more difficult, as the lines between permitted and not permitted behaviors became harder to define. (Photo courtesy of Steve McCaw)



Toohar, the former prosecuting/investigatory attorney with the New York Ethics Commission, had plenty of tales from the front lines to share with the audience. She was so warmly received when she spoke at last year's Ethics Day that Androphy invited her back for more. "In a time when there are not many heroes," Androphy said of her, "Meave is mine." (Photo courtesy of Steve McCaw)





*The award-winning NIEHS Office of Ethics team gathered on the patio, after another successful Ethics Day program. Shown, left to right, are Patricia Harris, D.J. Joya, Bledsoe, Androphy, Jackie Stillwell, Stephen Copeland, and Resnik. (Photo courtesy of Steve McCaw)*

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

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## NIEHS gears up for Rio+20

*By Eddy Ball*

NIEHS sponsored or co-sponsored two events, during May, related to the upcoming [Rio+20 United Nations Conference on Sustainable Development](#) June 20-22 in Rio de Janeiro. The events focused on global environmental health and the developmental origins of health and disease.

The NIEHS lead for both events was Senior Advisor for Public Health John Balbus, M.D. As part of the preparation for Rio+20, NIEHS held a regional meeting of the World Health Organization/Pan American Health Organization (WHO/PAHO) Collaborating Centers in the area of [Sustainable Development and Environmental Health](#) Oct. 24-26, 2011 ([see story](#)).



**RIO+20**  
United Nations  
Conference on  
Sustainable  
Development

**Linked video:**

[Watch as U.N. officials and conference participants discuss the road to Rio+20 \(04:03\)](#)

(Launches in new window)

Download Media Player: Flash

“The goal of NIEHS involvement in these global forums is to promote our science in a number of areas, including indoor and outdoor air pollution, green chemistry, and water contamination, in an international forum that can set the path for global improvements in public health,” Balbus explained. “By partnering with international organizations like the World Health Organization, we can help ensure that decision makers in the realms of sustainable development are aware of the significant health implications of their actions.”

## Institute of Medicine (IOM) Roundtable

NIEHS sponsored an IOM [Roundtable on Environmental Health Sciences, Research, and Medicine](#) virtual meeting May 9 on “Global Sustainable Development and Environmental Health: A Conversation Around the 2012 Rio+20 United Nations Conference.” The program featured a webinar of presentations on the interactions between health and sustainable economic growth.

In their keynote talks, Balbus discussed “[Environmental Health Goals and Indicators for Sustainable Development](#)”; Maria Neira, M.D., of WHO, presented an “Overview of How Health Contributes to Advances in Sustainable Development and Economic Growth”; and Akiko Maeda, Ph.D., of the World Bank, answered the question “Is an Investment in Health Also an Investment in Development?”

## Defining environmental health indicators for Rio+20

At a separate event held in conjunction with WHO, NIEHS co-sponsored an expert consultation May 17-18 in Geneva on health indicators for sustainable development. The focus of the consultation was the role of health indicators in monitoring and evaluating performance of sustainable development decisions, as well as in contributing to the governance of sustainable development.

The discussions laid the foundation for a framework for developing and applying health indicators related to seven critical issues being emphasized in the Rio+20 discussions — decent jobs, energy, sustainable cities, food security and sustainable agriculture, water, oceans and disaster readiness. Overall, the group worked to identify issues linking health, on the one hand, and economic development, poverty reduction, consumption, and production and identify a suite of indicators based on available and reliable sources of data on a global basis.

The meeting closed with the development of briefing documents containing a list of health indicators, which WHO’s Director General Margaret Chan will deliver at the Rio+20 conference. This consultation and set of documents is just the beginning of a process to set long term sustainable development goals and monitor progress towards them.

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## Sandler honored by public health society

*By Eddy Ball*

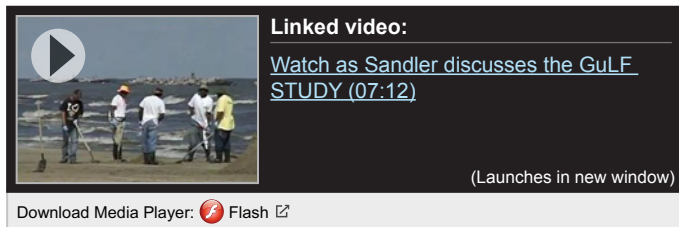
NIEHS epidemiologist [Dale Sandler, Ph.D.](#), has been elected as an alumni member of the Alpha Chapter of the Delta Omega Honorary Society in Public Health at the Johns Hopkins Bloomberg School of Public Health, where she earned her doctorate. New student, faculty, and alumni members were formally recognized May 15 in Baltimore at the Alpha Chapter’s Annual Dinner and Induction Ceremony.



*“If we look back to 1992, when the Rio conference talked about development without considering sustainability, it’s clear we’ve come a long way,” Balbus said. “Now the challenge is to establish public health and primary prevention as cornerstones of the framework for achieving sustainable development in 2012 and beyond.” (Photo courtesy of Steve McCaw)*



Sandler is head of the NIEHS Epidemiology Branch and a lead researcher on several large, high profile prospective studies, including the [Sister Study](#), the [GuLF STUDY](#) (Gulf Long Term Follow-Up Study), and the [Agricultural Health Study](#). She joined NIEHS in 1979 and was appointed head of the Epidemiology Branch in 2003, after serving two years as acting chief.



### Recognized for advancing public health

In her April 24 message announcing Sandler's election, Delta Omega Alpha Chapter President Carolyn Fowler, Ph.D., congratulated Sandler and underscored the society's high membership standards.

"Only faculty and alumni meeting the highest academic standards and endorsed by the faculty are eligible for membership, and only those demonstrating a potential for significant contribution to the field of public health are elected to the society," Fowler wrote. "Election to membership in Delta Omega recognizes not only merit, but also encourages further excellence and devotion to public health."

[Delta Omega](#) was founded by two graduate students at The Johns Hopkins University School of Hygiene and Public Health in May 1924, at a time when public health, as a profession, was still in its infancy and the graduate schools of public health had only recently come into being. Despite some trying times, especially during World War II and the 1950s, the society has expanded nationally to 59 local chapters at the nation's leading schools of public health, with about 6,000 members recognized for their exceptional academic and professional achievements.

### A distinguished career in public health and epidemiology

Election to Delta Omega is the latest in a long list of honors Sandler has received for her work in epidemiology and public health.

Sandler was elected as a fellow of the American College of Epidemiology and as a member of the American Epidemiological Society. In addition, the American College of Epidemiology presented her with its Leadership and Distinguished Service Award and its Leadership Recognition. In 2010, she received the U.S. Environmental Protection Agency Office of Research and Development Honor Award, a Bronze Medal team award.

NIH and NIEHS have recognized Sandler with several Director's Awards, most recently for her work on the Gulf Oil Spill. In 2010, her peers in the NIEHS Division of Intramural Research selected her as Scientist of the Year.

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*Sandler recognized the need for the GuLF STUDY, soon after the explosion and fire on the Deepwater Horizon in April 2010.  
(Photo courtesy of Steve McCaw)*

# Postdocs and apprentices wow middle school students

By Ed Kang

Since early February, NIEHS fellows and other staff have volunteered at Lowe's Grove Middle School in Durham, N.C., as part of a unique apprenticeship program called [Citizen Schools](#). The project "Healthy Lungs, Happy Living," partnered low-income, middle school students with local scientists, to gain hands-on experience in environmental health. After an intensive 10-week immersion, the young apprentices showed off their new knowledge May 3 for parents, family, friends, and the community in a public showcase called WOW!

## Developing environmental ambassadors

Nisha Cavanaugh, Ph.D., who served as one of the project coordinators, was the initial driving force for getting NIEHS staff involved in the program, in part to fulfill a desire to be closer to the community in NIEHS' backyard. Biologist Mercedes Arana, Ph.D., who was a project coordinator and one of the principal instructors, said, "The 'Healthy Lungs, Happy Living!' apprenticeship has given us an opportunity to teach what we know and love, and lead these students through a stimulating journey."

During the WOW! event, the apprentices, under the tutelage of their volunteer coaches, showcased what they learned at four stations, to measure lung capacity, visualize oxygen and carbon dioxide using phenol red, demonstrate how the lungs work, and describe the relationship between asthma and the environment.

"The 10-week program has given these environmental ambassadors a sneak peek at science, and it's provided them an opportunity to teach back to their friends and family what they've learned," said Arana.

In addition to teaching at Lowe's Grove once a week, Cavanaugh, Arana, and the other volunteers had to create meaningful lesson plans and develop teaching materials. In fact, their preparations began in September 2011 with the decision to develop the theme "Healthy Lungs, Happy Living." Each week's lesson represented a unique enrichment activity, which was taught during the after-school program for sixth- to eighth-graders.

The first four weeks taught students about the respiratory system, how air pollution affects lung function, and how lungs function in the body. Next, the students built mechanical lungs, and learned about the effects of



*NIEHS Deputy Scientific Director Bill Schrader, Ph.D., left, showed his support of the program and volunteers, most of them from the NIEHS Division of Intramural Research. After an evening of spirited discussion, he remarked, "I don't know who smiled the most — the young scientists or their NIEHS teachers." (Photo courtesy of Steve McCaw)*



*The students became the teachers, as they explained to friends, family, and faculty the relationship between happy lungs and happy living. (Photo courtesy of Steve McCaw)*



smoking on lung health and of asthma as a respiratory disease. The last three weeks, they spent preparing for the WOW! event — honing their presentation skills and demonstrating their new knowledge.

In all, nearly 20 NIEHS staff members, representing several divisions of the Institute, took part in the program to raise awareness of the importance of environmental health through a curriculum of instruction and hands-on learning activities. A scientist from the U.S. Environmental Protection Agency (EPA) also joined the group.

Additionally, the effort benefited from financial support by the NIEHS Office of Science Education and Diversity (OSD), and resources offered by the Environmental Health Perspectives (EHP) Science Education Program. OSD Director Ericka Reid, Ph.D., said of the program, “We are hopeful that this kind of activity is just the beginning for NIEHS, as we seek to engage the next generation of environmental health scientists.”

Volunteers in the Lowes Grove Middle School program included the following:

**NIEHS Trainees:**

April Binder, Ph.D.  
Ashley Godfrey, Ph.D.  
Bret Freudenthal, Ph.D.  
Danielle Watt, Ph.D.  
Darshini Trivedi, Ph.D.  
Jen Nichols, Ph.D.  
Jon Ciencewicki, Ph.D.  
Julie Lowe, Ph.D.  
Kirsten Verhein, Ph.D.  
Kristin Lichti-Kaiser, Ph.D.  
Michelle Heacock, Ph.D.  
Nisha Cavanaugh, Ph.D.  
Shay Covo, Ph.D.  
Tim Gingerich

**NIEHS Staff:**

Mercedes Arana, Ph.D., biologist  
Elena Braithwaite, Ph.D., staff scientist  
Sharon Beard, industrial hygienist  
Ed Kang, public affairs specialist

**EHP:**

Bono Sen , Ph.D.

**EPA:**

Gayle Hagler, Ph.D.

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

## Citizen Schools

The NIEHS scientists are part of a nationwide program that has proven its worth by boosting participants’ success rates. According to Citizen Schools follow-up since 2002, young people who were part of the program attend classes more often, outperform their peers in six measures of student success, are 20 percent more likely to graduate from high school, and are 80 percent more likely to attend college.

Since its start by former college roommates Eric Schwarz and Ned Rimer in 1995, Citizen Schools has spread to 18 cities throughout the nation, providing hands-on learning taught by AmeriCorps educators and [volunteer experts](#) from all fields — from science and law, to finance and community service. The program operates in 31 schools and has served 4,500 students through the efforts of 4,200 volunteers.

In a message to the NIEHS Citizen Schools team, Sarah Rabiner, national teaching fellow and academic program lead of the Citizen Schools at Lowe’s Grove Middle School, congratulated the team on its outstanding program. “A huge thanks to you all for creating and leading the best apprenticeship I have supported in my time at Citizen Schools,” she wrote. “It was beyond a pleasure to work with such a dedicated group of volunteers who are so committed to the students.”

“Know that you set the bar very high for any future group!” Rabiner added. “You should be so proud of the work that you did. Those of you who made it to the WOW! saw the impact on students — they were flawless presenters!”



*Anton Jetten, Ph.D., head of the NIEHS Laboratory of Respiratory Biology, left, showed that he knows a thing or two about pulmonary function in the lung capacity demonstration. (Photo courtesy of Steve McCaw)*



*Arana not only brought her knowledge to the program, but also her passion for inspiring the next generation of scientists. Clearly, her enthusiasm is contagious! (Photo courtesy of Steve McCaw)*



*Nichols, second from left, and Verhein, second from right, were heavily involved in prepping students for their WOW! presentations. (Photo courtesy of Steve McCaw)*



*Cavanaugh, who has been involved in NIEHS postdoc activities as part of the NIEHS Trainees Assembly, was instrumental in the Institute's involvement in the Citizen Schools program. (Photo courtesy of Steve McCaw)*





*Students and volunteer instructors enjoyed a moment of levity, as 10 weeks of intense preparation and practice came to fruition. (Photo courtesy of Steve McCaw)*

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## NIH Center for Regenerative Medicine launches website

*By Eddy Ball*

Scientists with an interest in the clinical translation of stem cell-based technologies now have an additional online resource with the launch of a new [website](#) by the NIH Center for Regenerative Medicine (NIH CRM). The NIH CRM is an initiative of the NIH Common Fund and is administered by the [National Institute of Arthritis and Musculoskeletal and Skin Diseases](#).

The NIH CRM provides several important services, including the following:

- Facilitating the generation of induced pluripotent stem cells, as well as the derivation or isolation of other types of stem cells.
- Making available a range of adult stem and progenitor cell populations, as well as the protocols and standard operating procedures used for their derivation, culture, and differentiation.
- Providing services and information to both the intramural and extramural NIH communities that facilitate the use of stem cell technologies for therapeutic purposes and for screening efforts.



*Rao was chosen last year to create a world-class center of excellence in stem cell technology. He is internationally renowned for his research involving human embryonic stem cells and other somatic stem cells. (Photo courtesy of NIH)*

- Collaborating in the U.S. and internationally with partners and stakeholders, including governments, research institutions, and commercial entities, to ensure that efforts are coordinated, and standard policies are in place, to minimize roadblocks to advancing stem cell technologies.

Headed by Director [Mahendra Rao, M.D., Ph.D.](#), the NIH CRM has a program manager and operations coordinator to facilitate work by affiliated faculty housed at a range of NIH Institutes and Centers. NIEHS is represented by lead researchers [Trevor Archer, Ph.D.](#), head of the Laboratory of Molecular Carcinogenesis; [Anton Jetten, Ph.D.](#), head of the Laboratory of Respiratory Biology; and [Raja Jothi, Ph.D.](#), head of the Biostatistics Branch Systems Biology Group.

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## Future NIH management leaders visit NIEHS

*By Kimberly Thigpen Tart*

A cadre of future NIH science management and policy leaders made a trek April 23 from Bethesda, Md., to North Carolina. Eighteen Presidential Management Fellows (PMFs) and NIH Management Interns (MIs) traveled to NIEHS to learn about the Institute and its programs, and speak with staff about potential intern rotations.

The Presidential Management Fellowship is a federal government-wide program that NIH has participated in since 1985. NIH PMFs develop rotational assignments across the various institutes and centers (ICs), in a broad range of administrative and programmatic research support areas, including budget and finance, outreach and communications, information technology, grants management, program and management analysis, contracts management, human resources, and general administration. These rotational opportunities provide on-the-job training with exposure to senior leadership.

The NIH Management Intern program was established in 1957 and has trained over 400 interns. The program offers the opportunity for highly motivated NIH employees to explore different administrative fields, gain invaluable insight into science management, and change careers within NIH.

### Getting the NIEHS perspective

During their visit, the PMFs and MIs were given an overview of NIEHS history and current strategic planning efforts by Kimberly Thigpen Tart, J.D., and Sheila Newton, Ph.D., and viewed a video on the field of environmental health, created by the American Public Health Association for the 100th anniversary of its Environment Section, which features many NIEHS grantees. The visitors then had an opportunity to meet and hear the career stories of former PMFs and MIs who are now working at NIEHS, including Liam O’Fallon, Jerry Phelps, Jim Remington, and Molly Puente from the Division of Extramural Research and Training, as well as Dona McNeill, Chris Long, and Joellen Austin from the Office of Management.

After a walking tour of the Institute, led by John Schelp of the Office of Science Education and Diversity, and lunch in the cafeteria, the interns learned about some of the Institute’s unique programs through presentations by senior staff. Presenters included Liam O’Fallon on the Partnerships for Environmental Public Health program; Kris Thayer, Ph.D., on the NTP Office of Health Assessment and Translation; Stavros Garantziotis, M.D., on the Clinical Research Unit; Jim Remington on the Worker Education and Training Program and Deepwater Horizon efforts; and Jane Schroeder, Ph.D., on the NIEHS journal *Environmental Health Perspectives*.



The day was rounded out with a presentation and driving tour of the area, hosted by Tina Valdecanas of the Research Triangle Foundation of North Carolina.

### **Positive outcomes**

MI Ned Culhane wrote in an email, following the visit, “The wide variety of sessions and staff with whom we interacted provided a unique perspective into the Institute and its culture.” PMF Caroline Sonnefeld wrote, “The trip was well received by all of the interns and I’m sure you’ll see some of us in North Carolina for rotations.” The NIEHS Bethesda office is currently hosting PMF Maya Levine in a policy rotation.

NIEHS Executive Officer Joellen Austin, whose office sponsored the trip, says that the visit was important because “It provides up-and-coming leaders at NIH insight into who we are and what we do here, that they might not otherwise get because we’re not on NIH’s main campus. It’s a good recruitment tool, as well as another way to keep NIEHS integrated with all of the other NIH ICs.”

(Kimberly Thigpen Tart, J.D., is a program analyst in the NIEHS Office of Policy, Planning, and Evaluation.)



*Future leaders joined their hosts on the NIEHS patio. (Photo courtesy of Steve McCaw)*

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# SRP graduate student receives prestigious fellowship

*By Angela Spivey*

David Ciplet, a graduate student in the Brown University Superfund Research Program (SRP), has received a prestigious [Switzer Environmental Fellowship Program](#) award. Ciplet is one of 20 students, nationwide, selected to receive the fellowship in 2012, and one of three students from the Brown University SRP Community Engagement Core to receive it in recent years.

Switzer Fellows are highly talented graduate students in New England and California whose studies are directed toward improving environmental quality and who demonstrate the potential for leadership in their field. Ciplet will receive a cash award to support his graduate study, as well as networking and leadership support from the foundation.

“I feel both honored and extremely fortunate to be included as part of this network of change-makers,” Ciplet said. “It is inspiring to be among such a dedicated and accomplished group.”

The previous SRP students who received a fellowship from the Switzer Foundation were Laura Senier, Ph.D., who won the fellowship in 2007, and Elizabeth Hoover, Ph.D., who received it in 2008.



*Switzer Environmental Fellowship Program awardee David Ciplet (Photo courtesy of David Ciplet)*

Senier is an assistant professor at the University of Wisconsin-Madison. Her research focuses on the causes for common, complex diseases, such as cancer, heart disease, and diabetes that are impacting public health science and policy in the United States. Hoover remained at Brown and is now an assistant professor of American studies and ethnic studies. Her research interests include environmental health and subsistence revival movements in Native American communities.

## Encouraging equitable environmental policy

Ciplet is a member of the Contested Illnesses Research Group at Brown, which studies the formation and impact of social movements related to health, such as disputes over environmental causes of asthma, breast cancer, and Gulf War illnesses. Ciplet said that the group has been a critical support structure in his own work, in which he aims to conduct research that encourages more equitable and effective environmental policy. “Much of my research, to date, has generated knowledge about how international climate change policy can more adequately support developing countries in their efforts to adapt to climate change impacts,” Ciplet said.

Ciplet has also focused on domestic policy. His dissertation research is focused on factors that are enabling and constraining a transition to more sustainable energy policy in the United States. “Like my research on international climate change policy, I seek to contribute knowledge that is both timely and accessible, in order to encourage more effective policy on this issue,” he said.

## Involving students in environmental justice

In addition, Ciplet hopes to find ways for students to engage in local and global efforts for environmental justice. As a research assistant in the SRP Community Engagement Core, Ciplet leads a coordination team of



Brown University students who support numerous environmental health and justice initiatives. The team is preparing for its fourth summer with the Community Environmental College, a free 8-week program at Brown that educates teenagers on environmental justice issues, including toxicants, air pollution, waste, food, and climate change.

Ciplet said that the Switzer fellowship will help him in realizing all those goals. “I believe that the unique support structure and social networks that Switzer provides will enable me to progress in making both aspects of this vision a reality. This fellowship will enable me to develop the skills, knowledge base, and experience needed to serve as an effective bridge between local community struggles for environmental health and justice, and broader political processes intended to generate solutions to complex environmental problems.”

(Angela Spivey is a contract science writer for the NIEHS Superfund Research Program.)

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## WETP assembles DOE safety and health trainers

*By Dusty Russell*

The NIEHS Worker Education and Training Program (WETP) hosted a National Trainers’ Exchange May 7-8 in Knoxville, Tenn., for safety and health trainers funded under its U.S. Department of Energy (DOE) Nuclear Worker Training Program. More than 100 hazardous material (HAZMAT) and radiation (RAD) safety and health trainers, who are responsible for annually training some 35,000 workers engaging in environmental restoration activities at DOE nuclear weapons sites, came together to share best practices and new techniques, to increase training effectiveness across the DOE complex through a series of workshops conducted by the trainers themselves.

WETP Public Health Educator Ted Outwater opened the meeting by noting the importance of the partnership between NIEHS and DOE in achieving the goal of a safer HAZMAT and RAD workforce at DOE sites. “We recognize the valuable contributions of effective trainers to this goal,” he said. “NIEHS wants to encourage an ongoing dialogue, to address the persisting challenges to ensuring DOE worker safety through mechanisms such as the Trainers’ Exchange.”

Trainers from the eight consortia, funded by NIEHS through the DOE Nuclear Worker Training Program, led four workshops — advanced training technologies, instructor development, training challenges, and technical updates.

Instructor development workshops provided up-to-date information about recent changes in training requirements, and other pertinent trends and issues related to safety training at DOE sites. Significant attention was allotted to discussions and exercises related to hazard identification, systems of safety, the hierarchy of prevention and control, and strategic preventative measures to address areas of concern.



*Beard, right, led several panels that shared new training strategies and best practices with colleagues from throughout the U.S. (Photo courtesy of Jim Remington)*

In the closing segment of the meeting, attendees expressed their appreciation to NIEHS for hosting the event. Trainers noted that, while the challenges continue, they felt more empowered and encouraged in their goal to improve their safety programs. As WETP Industrial Hygienist Sharon Beard commented in closing the workshop, “There is clearly no shortage of innovation among us, and together we can exponentially improve worker safety across the DOE complex.”

Participating organizations included the International Union of Operating Engineers, Laborers’ International Union of North America (LIUNA) Training and Education Fund, International Chemical Workers Union (ICWU), United Steelworkers (USW), International Association of Fire Fighters, Center for Construction Research and Training (CPWR), International Brotherhood of Teamsters, and the Community College Consortium for Health and Safety Training under the National Partnership for Environmental Technology Education (PETE).

(Dusty Russell is a public health specialist with MDB, Inc., a contractor for WETP.)

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*Patricia Aldridge reported back lessons learned from the front lines after a small group activity. Aldridge is the training manager for the Hazardous Materials Management and Emergency Response Mission Support Alliance in Hanford, Wash. (Photo courtesy of Jim Remington)*



# Science Notebook

## Seminar addresses developmental origins of immune disease

By Heather King

Biochemist Paige Lawrence, Ph.D., delivered a guest lecture April 26 at NIEHS, hosted by NIEHS Health Scientist Administrator Mike Humble, Ph.D. Her talk, “Developmental exposures, epigenetics, and the immune system” addressed the relationship between environmental agents and defects in the immune system that she has identified in the course of her [NIEHS-funded](#) research.

Lawrence is a professor at the University of Rochester Medical Center School of Medicine and Dentistry where she holds appointments in both Environmental Medicine, and Microbiology and Immunology. The research [Lawrence](#) presented focused on how maternal dioxin exposure during pregnancy can alter the immune response of a developing fetus or newborn and lead to increased rates of respiratory infection. Dioxins are found in cigarette smoke and are a common environmental pollutant, and understanding the biological mechanisms behind their adverse effects on human health is a major NIEHS [initiative](#).

### A focus on dioxins

While Lawrence has also studied the immune effects of other environmental agents, such as bisphenol A (BPA) and neonatal oxygen supplementation, her talk focused on dioxins and other molecules that bind the aryl hydrocarbon receptor (AhR). The AhR is a biological sensor that binds toxins and, in response, stimulates the expression of various proteins, including toxin-metabolizing enzymes and cytokines, which regulate the immune system.

By treating mice with the classic dioxin 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) at low, environmentally relevant doses, Lawrence’s group has been able to observe an altered immune response while maintaining a functional, intact immune system.



*Following her talk, Lawrence answered questions on topics ranging from the long-term effects of in utero dioxin exposure, about which little is known, mechanistically, to AhR ligands. (Photo courtesy of Steve McCaw)*

### Mutants show the AhR receptor is key, not nurturing behaviors

To connect the impaired immune response in mouse pups to dioxin exposure, researchers in the Lawrence laboratory repeated their experiments with pups lacking the dioxin receptor, AhR.

They found offspring that do not produce dioxin receptor, do not exhibit immune defects with maternal dioxin exposure, establishing the critical role of AhR in the altered immune function and the specific AhR-based pathway of impaired immunity. The experiments also show changes in maternal nurturing behaviors that could result from exposure are not a factor, because exposed mothers produce pups without immune defects when those pups lack AhR.

## Increased susceptibility to influenza

After treating pregnant mice with TCDD, researchers exposed the offspring to mouse-adapted influenza A virus. Compared to the offspring of unexposed mice, the dioxin-exposed mice produced fewer virus-targeting cells and had an overall weakened immune response.

The timing of maternal exposure was also relevant, with dioxin exposure during the later stages of pregnancy and the early postnatal period causing a more significant reduction in immune response.

## Effects on offspring follow bone marrow graft

Notably, the dioxin-altered immune response Lawrence observes can be transferred from animal to animal, by transplanting the immune precursor cells found in bone marrow. Her research group demonstrated this by performing bone marrow transplantation between exposed and unexposed mouse pups. The dioxin-induced immune defects follow the grafts, showing that biological changes in the basic immune cells are the source of the defective response.

## Evidence for epigenetic changes in immune cells

Though epigenetic regulation of the immune system is not well studied, Lawrence decided to investigate the possibility that such changes, which include DNA methylation and histone modifications, are factors in the immune response to maternal dioxin exposure. To properly evaluate epigenetic changes, researchers in her group had to first sort specific types of immune cells, from the lymph nodes of exposed and unexposed mice, into groups. This labor-intensive project paid off, by showing that significant changes in DNA methylation go along with the dioxin-induced immune changes she has observed.

Lawrence found that a specific type of immune cell, the CD8<sup>+</sup> T cell, shows interesting changes in the levels of a key DNA methyltransferase. Preliminary results also show differences in global DNA methylation patterns between the offspring of dioxin exposed versus unexposed mice. To perform global studies of DNA methylation changes, Lawrence is working in collaboration with professor Lee Kraus, Ph.D., of the University of Texas Southwestern Medical Center. Together, they are studying epigenetic changes across the genome in CD8<sup>+</sup> T cells, and other immune cells, following maternal dioxin exposure. These studies and others in Lawrence's laboratory promise to bring new attention to epigenetic changes that play a role in the immune response, especially changes resulting from environmental exposures.



*Lawrence spoke before a large audience from the NIEHS Division of Intramural Research, as well the Division of Extramural Research, which hosts the Keystone Science Lecture Seminar Series. (Photo courtesy of Steve McCaw)*



*Humble moderated the question and answer session that followed Lawrence's talk. He specializes in the immune response to environmental exposures and administers the funding that supports Lawrence's work. (Photo courtesy of Steve McCaw)*



The Keystone Science Lecture Seminar Series gives NIEHS-supported investigators, such as Lawrence, the opportunity to present findings about environmental exposures that affect human health.

(Heather King, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Structural Biology Protein Expression Core.)

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## Cellular damage from normal metabolism potentially causes cancer

By Robin Arnette

Individual mutations, or changes to an organism's DNA, are thought to be rare events that occur randomly, but new [research](#) from a team led by NIEHS scientists has identified DNA regions in yeast and in some cancers that have a disproportionately high number of mutations. These mutation clusters arose simultaneously, and are produced by exposure to environmental toxins and through typical biochemical processes that occur in living cells. The findings represent an exception to the traditional view that mutations accumulate over time and may explain one of the mechanisms behind cancer development.

Investigators from NIEHS, The Broad Institute of MIT and Harvard, and the Lineberger Comprehensive Cancer Center at the University of North Carolina at Chapel Hill published the work online May 17 in the journal *Molecular Cell*. The journal also selected the paper as the featured article.

### Discovery in a yeast model

Dmitry Gordenin, Ph.D., a senior associate scientist in the NIEHS Laboratory of Molecular Genetics (LMG) and corresponding author on the paper, said the discovery resulted from work in a yeast model system designed to investigate mutations caused by environmental damage. Team members subjected yeast to continuous damage, by growing them in media that contained the carcinogen methyl methanesulfonate (MMS). After sequencing the genomes, or total DNA, of approximately 70 yeast cells that emerged after MMS treatment, they found that the number, distribution, and pattern of mutations far exceeded expectations.

"Normally, mutations occur haphazardly throughout the genome, and there is no rule by which [nucleotide] bases are changed, but we found that certain patches, i.e., clusters, contained more mutations than the rest of the genome," Gordenin said. "These clusters also exhibited a very unusual pattern, suggesting they were formed at the same time in stretches of abnormally long single-stranded DNA."



*Gordenin said that he and his group are working with bioinformatics experts on future studies. They plan to develop tools that will dissect the history and mutation mechanisms operating in specific cancers by extracting the information from published sequence data and from cancer sequence databases. (Photo courtesy of Steve McCaw)*

## Mutation clusters in human tumors

Gordenin and his team wondered if they could use the same principle to see if a similar phenomenon occurred in human cancers. At the time, hundreds of thousands of cancer mutations were being published in the scientific literature, so the team developed bioinformatics tools to look for mutation clusters in 32 human tumors. The tumors belonged to three different cancer types — head and neck, prostate, and multiple myeloma, which is cancer of the antibody-producing white blood cells. The scientists were surprised to find a little over half of the cancers also had mutation clusters.

“We found that in cancer, the cause of the mutation clusters wasn’t environmental damage like we saw in yeast,” explained Steven Roberts, Ph.D., an NIEHS postdoctoral fellow and first author on the paper. “The DNA sequence surrounding clustered mutations suggested that specific proteins called APOBEC cytosine deaminases that contribute to our natural defenses against viruses somehow damage our DNA. APOBEC proteins are stimulated via Toll-like receptors and interferons to inactivate viruses attacking our body. Our work suggests that they are also mutating our chromosomal DNA. Thus, damage is coming from our normal physiology.”

Michael Resnick, Ph.D., is a co-author on the study and leads the LMG [Chromosome Stability Group](#) at NIEHS. He said, “Researchers have always considered that mutagenic lesions in the DNA of an organism could be caused by normal metabolism and that these lesions could contribute to genetic damage observed in the cancer genome. Now, we see a clear example supporting this hypothesis.”

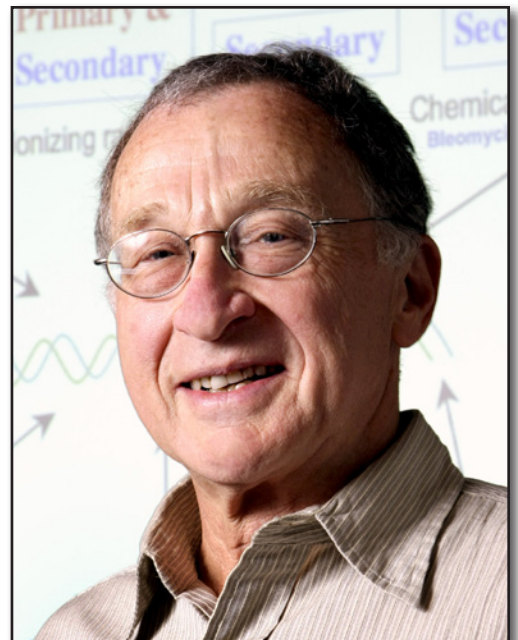
Importantly, the NIEHS-led study was published online the same day as a Cell [paper](#) from a Wellcome Trust Sanger Institute team in the United Kingdom. The Sanger team studied 21 breast cancer samples and made similar conclusions about mutation clusters and the involvement of APOBEC enzymes.

## Utilizing NextGen sequencing

Gordenin said that the results of both teams were only possible due to the advancements of Next Generation (NextGen) sequencing that happened in recent years. He hopes the technology and accumulating information stored in other NextGen databases, such as The Cancer Genome Atlas (TCGA), a major cancer database managed by the National Cancer Institute and the National Human Genome Research Institute, will allow him to hunt for mutation clusters in sequences from thousands of additional tumors and normal human tissue. The work may provide an understanding of the role of clustered mutagenesis in human disease and highlight exposures that damage the human genome. The immediate implication from the current study is that several antiviral drugs capable of stimulating APOBEC genes, such as interferon-containing or interferon-stimulating drugs, should be looked at for potential long-term effects connected with enhanced mutagenesis.



*The research team is the first to report the existence of mutation clusters in yeast and cancers, and the first to determine that the mutations happen simultaneously. As first author on the paper, Roberts played a major role in the discovery. (Photo courtesy of Steve McCaw)*

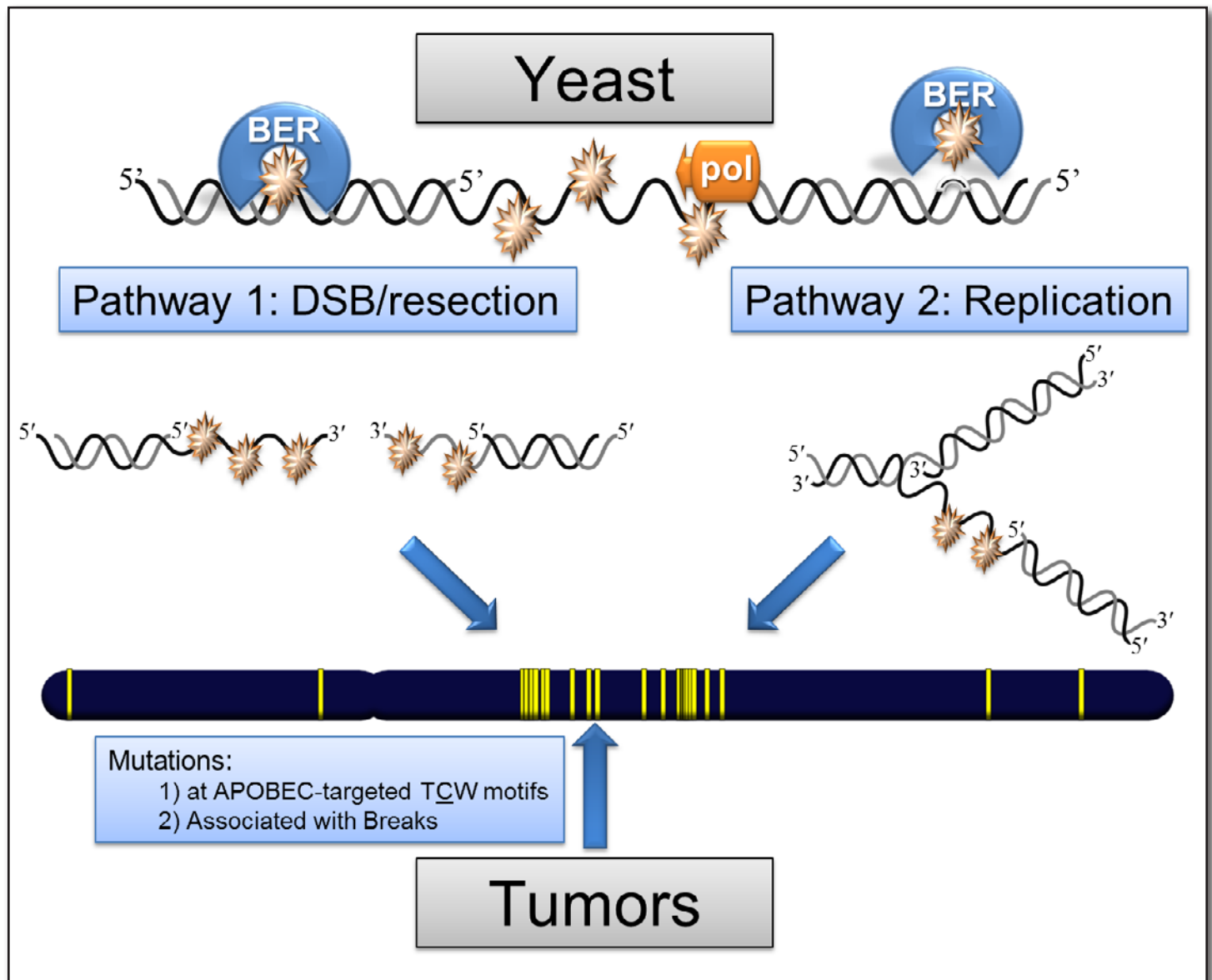


*Resnick's research group uses budding yeast and human cell models to study genome maintenance and natural environmental challenges to chromosome stability. (Photo courtesy of Steve McCaw)*



Gordenin said, “Looking at clusters is a productive way to explore the mechanisms that were acting when the cancer was emerging and developing. Our work shows the value of re-analyzing sequenced cancers to find things that no one has paid attention to before.”

*Citation:* Roberts SA, Sterling J, Thompson C, Harris S, Mav D, Shah R, Klimczak LJ, Kryukov GV, Malc E, Mieczkowski PA, Resnick MA, Gordenin DA. 2012. Clustered mutations in yeast and in human cancers can arise from damaged long single-strand DNA regions. Mol Cell; doi:10.1016/j.molcel.2012.03.030 [Online 17 May 2012].



**The mutation clusters phenomenon as demonstrated in yeast and in human cancers.** The DNA sequence surrounding clustered mutations in cancers suggested that specific proteins called APOBEC cytosine deaminases, which contribute to our natural defenses against viruses, somehow damage our DNA. (Graphic courtesy of Dmitry Gordenin)

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# Researchers explore transgenerational effects of ancestral exposures


By Eddy Ball

A new NIEHS-funded [study](#) offers more evidence about the transgenerational actions of environmental compounds on reproductive disease. The findings result from a productive collaboration between environmental researchers at Washington State University (WSU) and Department of Defense (DoD) scientists, and the DoD [Telemedicine and Advanced Technology Research Center](#).

The findings from a research team led by NIEHS [grantee](#) and WSU professor [Michael Skinner, Ph.D.](#), appeared online May 3 in the journal PLoS One. The paper outlines transgenerational effects similar to ones induced genetically, but are caused instead by epigenetic modifications of gene expression that do not alter DNA itself.




*Skinner spoke to an audience at NIEHS in 2011 about his lab's work. In an [interview](#) with Science Daily, he said of his group's findings, "What your great grandmother was exposed to when she was pregnant may promote ovarian disease in you, and you're going to pass it on to your grandchildren." (Photo courtesy of Steve McCaw)*



**Linked video:**

[Watch as Skinner discusses epigenetics and transgenerational inheritance \(07:18\)](#)

(Launches in new window)

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The team reports effects on adult-onset ovarian disease in F3 generation female rats, resulting from a direct exposure, experienced by F0 generation female rats and their F1 progeny, to a panel of five compounds and mixtures selected for their relevance to anticipated exposures by military personnel. An earlier [study](#) by the group, published Feb. 28 in PLoS One, found transgenerational disease in rats from exposure to all of the compounds used in the newest study.

While the evidence supports the notion that epigenetic modifications, triggered by environmental exposures, can result in transgenerational inheritance of disease — the so-called you are what your great-grandmother ate hypothesis — the researchers offered a caveat up front. “The current study used pharmacological doses and administration to assess potential transgenerational actions on ovarian disease, and should not be considered a risk assessment analysis.” However, they argue that, based on the significance of their findings, such a risk assessment analysis should be a follow-up to their study.

## Exposure during a critical window of development

The researchers studied five treatment groups of pregnant F0 outbred rats during days 8-15 of fetal development, a time of gonadal sex determination, exposed through injection to one of the compounds or mixtures, including a fungicide, a pesticide mixture, a plastic mixture, dioxin, and a hydrocarbon mixture ([see text box](#)). Because the researchers observed a drop in litter size for the F1 generation of the plastics group, they added another treatment group exposed to only half of the original dose.



The researchers injected only the original F0 pregnant females with the treatment compounds. F1 generation rats bred normally with other F1 animals of the same treatment group, generating F2 rats that were bred similarly to produce the F3 generation of animals.

The team evaluated ovaries taken from F0-F3 rats at one year of age, and the researchers performed microarray transcriptome analysis and methylated DNA immunoprecipitation to identify gene expression and epigenetic modification. They also performed confirmational experiments on cultured neonatal rat ovaries from four-day-old females.



*The Skinner Lab, on retreat in 2011, were obviously playing almost as hard as they've been working. (Photo courtesy of Michael Skinner)*

### **Ovarian abnormalities**

The team found increased numbers of ovarian cysts, a hallmark of polycystic ovarian disease, in all the treated lineage groups compared to control lineage groups. Mean decreases in the primordial follicle counts of 35 and 60 percent occurred in both the F1 generation, which was exposed across the placenta, and the F3 generation, which was exposed transgenerationally.

Although the researchers determined that treatment with the various toxicants can lead to different transgenerational phenotypes, all of the treatments resulted in the same increase in small ovarian cysts and the same decrease in the primordial follicle pool.

### **Public health implications**

In their call for further research, that they consider amply justified by the findings of their study, the authors conceded, “The current ovarian abnormalities and disease in rats cannot be directly correlated to the human polycystic ovarian syndrome nor human primary ovarian insufficiency and loss of fertility.”

Nevertheless, they add, there are compelling similarities between the morphological changes found in the rats and those found in the ovarian diseases that affect up to 18 percent of women, who often also experience insulin resistance and a higher risk for diabetes, in addition to infertility and other reproductive abnormalities.

“These results suggest a new paradigm be considered for the [genetic and epigenetic] etiology of [adult-onset] ovarian disease,” the researchers concluded. “Further elucidation of the etiology of ovarian disease and epigenetic transgenerational inheritance will provide insights into prevention and therapeutic strategies for female health.”

#### *Citations:*

[Manikkam M, Guerrero-Bosagna C, Tracey R, Haque MM, Skinner MK. 2012. Transgenerational actions of environmental compounds on reproductive disease and identification of epigenetic biomarkers of ancestral exposures. PLoS One 7\(2\):e31901.](#)

[Nilsson E, Larsen G, Manikkam M, Guerrero-Bosagna C, Savenkova MI, Skinner MK. 2012. Environmentally induced epigenetic transgenerational inheritance of ovarian disease. PLoS One 7\(5\):e36129.](#)

## A real life scenario of environmental exposure

According to the researchers, with valuable input from DOD, the team selected an exposure panel of widely used chemicals with some evidence of toxic, reproductive, or epigenetic effects in animals. The exposure compounds were the following substances and mixtures:

- Vinclozolin, an agricultural fungicide previously shown to cause transgenerational epigenetic disease
- A mixture of permethrin, the most commonly used human insecticide shown to have minor toxicologic effects in mammals, and DEET, an insect repellent reported to have negligible toxic effects
- A plastic mixture of bisphenol A (BPA), dibutyl phthalate (DBP), and bis(2-ethylhexyl)phthalate (DEHP), all plasticizer chemicals that commonly appear together in plastics with *in vitro* and *in vivo* toxic effects
- Dioxin (TCDD), a byproduct of some commercial chemical syntheses that has been shown to induce adult-onset diseases, including premature failure to exhibit estrous cycle activity
- Jet fuel (jet propellant 8, JP8), a hydrocarbon mixture often used for dust control on road surfaces, with known toxicologic effects, but not known to induce reproductive defects

The team used pharmacologic doses of all the compounds and mixtures.

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## p53 may affect susceptibility to cancer and other diseases

By Ashley Godfrey

In her seminar, “Adventures in polymorphisms and p53 function,” Wistar Institute professor [Maureen Murphy, Ph.D.](#), discussed her research on polymorphisms in the p53 protein. Murphy’s talk May 7 at NIEHS was hosted by Intramural Research Training Award Fellow [Kin Chan, Ph.D.](#), as part of the NIEHS Laboratory of Molecular Genetics (LMG) Fellows Invited Lecture Series.

“What’s especially exciting about Murphy’s work is her use of a humanized p53 knock-in mouse model to examine the effects of polymorphisms in p53 on multiple levels,” explained Chan. “As Maureen showed during her talk, two different alleles at amino acid 72 can give rise to very different health outcomes, as reflected by differences in susceptibility to diabetes, in effectiveness of immune function, and in female fertility.”



*As demonstrated by her many research accomplishments, Murphy has had a career-long interest in the mechanisms underlying cancer biology. “Why not study p53?” asked Murphy at the beginning of her talk. (Photo courtesy of Steve McCaw)*



## The p53 tumor suppressor

The p53 protein is crucial in multicellular organisms, where it regulates the cell cycle and is therefore involved in cancer prevention. As Murphy indicated in her talk, mutations in p53 are present in about 60 percent of all human tumors.

Research from Murphy's lab indicates that p53 suppresses tumor development, in part, through its ability to induce apoptosis, or cell death. In cells where DNA damage has occurred or where there is unscheduled cell proliferation, as there often is during cancer development, the p53 protein becomes stabilized and induces apoptosis in response to these and other cellular stresses.

Murphy and her lab are particularly interested in two different coding region polymorphisms, or single amino acid variants, in p53 and the impact these polymorphisms may have on the protein's ability to induce apoptosis. The first is more common in African-Americans than white Americans, substituting a proline residue at codon 72 (P72) for an arginine (R72), and the second is more rare, substituting a serine residue at codon 47 (S47) for a proline (P47). The S47 variant has only been found in the African-American population. Interestingly, the codon 72 variants also vary with geographic location. About 40 percent of people who live near the equator are homozygous for P72 but, higher up in latitude, the percentage drops and more people have the R72 variant.

"Since the P72 and S47 variants are more common in African-Americans this may help to explain ethnic disease disparities," stated Murphy.

## Using a unique mouse model to study different health outcomes

In order to understand how the codon 72 polymorphism could affect the function of p53, Murphy and her collaborators have created the first mouse model for this p53 polymorphism. Since the mouse p53 protein does not have this polymorphism, the knock-in mouse contains a humanized version of p53, encoding either the P72 or R72 variants. Murphy's research with this mouse model has shown that mice containing the P72 and R72 variants have significantly altered levels of apoptosis in different tissues.

By looking at the different gene transcriptional responses between the two variants, Murphy has shown that P72 and R72 respond dramatically differently to innate immunity stress. This difference is regulated by a subset of genes known to control the inflammatory response, including some of the NF- $\kappa$ B target genes, which are better activated by the P72 variant.



*Murphy was introduced by Chan on behalf of the LMG fellows and the LMG Trainee Action Committee (TAC). "We were thrilled that Maureen made the trip here to present the latest work from her group and to meet with researchers at the Institute," said Chan. (Photo courtesy of Steve McCaw)*



*Many members of the NIEHS community were on hand to hear Murphy present her seminar. Shown front, right to left, are Robert Langenbach, Ph.D., Michael Resnick, Ph.D., William Copeland, Ph.D., Jan Drake, Ph.D., Carl Anderson, Ph.D., and Joel Abramowitz, Ph.D. (Photo courtesy of Steve McCaw)*

“If P72 has a better response with innate immunity, then it might make sense why this variant is selected for near the equator where malaria and other infections are more common,” explained Murphy. In contrast, the R72 variant in people seems to be selected for in colder climates, and Murphy’s data suggests that R72 mice tolerate a diet rich in fat and sugar better, while P72 mice tend to develop diabetes on this regimen, which may explain the higher risk for diabetes in African-American populations.

Murphy concluded her talk with a brief look at her research on the other, less common p53 polymorphism. She has found that the S47 variant has impaired phosphorylation, which leads to decreased apoptosis. A better understanding of the role of these variants in disease should lead to improved diagnosis and treatment.

(Ashley Godfrey, Ph.D., is a postdoctoral fellow in the Molecular and Genetic Epidemiology Group in the NIEHS Laboratory of Molecular Carcinogenesis.)

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## Genistein exposure linked to abnormal immune response and infertility

*By Robin Arnette*

Previous research by NIEHS scientists determined that female mouse pups exposed to the plant estrogen genistein a short time after birth grew up to be barren. In their latest [work](#), the NIEHS team suggests that changes to the immune system are partly responsible for this genistein-induced rodent infertility.

Laboratory of Reproductive and Developmental Toxicology biologist [Wendy Jefferson, Ph.D.](#), and her colleagues working in the Reproductive Medicine Group headed by [Carmen Williams, M.D., Ph.D.](#), published their findings online in the May 2 issue of the journal *Biology of Reproduction*.

### Physiologic doses altered gene expression in mice

Jefferson treated female pups on postnatal days 1-5 with either corn oil as a control or 50 milligrams per kilogram per day of genistein, which exposes the mouse pups to the same amount of genistein present in the bloodstream of human babies following ingestion of soy-based infant formulas. She then examined the mice as adults, looking at gene expression in the oviducts, also known as the Fallopian tubes, which transport embryos to the uterus or womb.

She found that a large number of immune response genes were different in the genistein-exposed mice. Jefferson said her group also observed that half of their embryos died in the oviduct, and the ones that survived didn’t develop like the controls.

“We can’t for sure say the immune response changes caused the embryos to develop abnormally,” Jefferson maintained, “although we think it’s pretty likely.”



*Wendy Jefferson (Photo courtesy of Steve McCaw)*



Williams explained that if genistein caused the oviduct to become inflamed, it made sense that infertility would be the likely result.

“We know that in humans, inflammation of the oviducts greatly decreases the chance of a woman becoming pregnant because fluid from the inflamed tubes hurts the embryos,” she said.

Intake of relatively low levels of plant estrogens occur through the diet, but much higher amounts can be ingested through nutritional supplements or soy-based infant formulas. Because the human reproductive tract develops over a long period of time, beginning in the womb and continuing into adolescence, the study’s results suggest that exposure to high plant estrogen levels during these times of development could affect fertility in women.

*Citation:* Jefferson WN, Padilla-Banks E, Phelps JY, Cantor AM, Williams CJ. 2012. Neonatal phytoestrogen exposure alters oviduct mucosal immune response to pregnancy and affects preimplantation embryo development in the mouse. Biol Reprod; doi:10.1095/biolreprod.112.099846 [Online 2 May 2012].

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Carmen Williams (Photo courtesy of Steve McCaw)

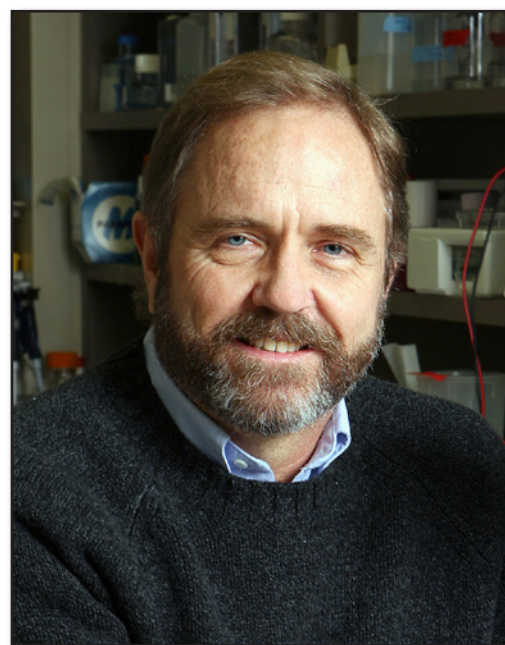
## Researchers pinpoint key protein that protects against septic shock

By Cindy Loose

Patients with simple urinary tract infections may be protected from more severe infections and even death by just one microscopic protein in one specific class of white blood cells.

That startling insight, which also may apply to other types of bacterial infections, is one of a number of findings from a recent [study](#) by three NIEHS scientists. Various types of bacterial infections, including those caused by Gram-negative bacteria, have become increasingly menacing as more and more of them become resistant to existing antibiotics.

Led by NIEHS lead researcher Perry Blackshear, M.D., D.Phil., the team showed that life-threatening septic shock was abnormally likely when low doses of a Gram-negative bacterial toxin were injected into mice that were genetically engineered to lack the protein tristetraproline (TTP) in myeloid cells, a major class of white blood cells. This was true even though only myeloid cells were altered to lack TTP.



This study is the latest of more than 235 peer-reviewed papers Blackshear has published in leading biomedical journals. (Photo courtesy of Steve McCaw)

## Exploring differences in host susceptibility

The study is part of a larger, decades-long project that is exploring the differences in susceptibility to infection among individuals, particularly how that susceptibility is related to a deficiency in TTP production. The project is also aimed at identifying small molecules that could be used in developing drugs to increase TTP amounts or actions.

“The body has a very complicated way of dealing with the primary response to infection,” said Blackshear. “In some cases, when a simple infection occurs, the body responds in overwhelming ways that can be fatal.”

TTP, a focus of the NIEHS team studying differential susceptibility to infection in individuals, is both an anti-inflammatory protein and an anti-Tumor Necrosis Factor (TNF) protein. An excess of TNF has been implicated in a number of chronic diseases, including autoimmune diseases such as rheumatoid arthritis and Crohn’s disease, as well as in the more acute septic shock syndrome caused by infections.



*Qiu was first author on the study. (Photo courtesy of Steve McCaw)*

## Genetically engineered mouse lacks TTP

Previous studies have shown that mice genetically engineered to lack TTP develop early-onset, severe inflammatory indications, including extreme drops in weight, arthritis, inflammation of the left heart valves, myeloid hyperplasia, and autoimmunity.

Blackshear, in collaboration with two members of the Polypeptide Hormone Action Group, research fellow Lian-Qun Qiu, Ph.D., and staff scientist Deborah Stumpo, Ph.D., advanced the work at NIEHS by genetically engineering a mouse in which TTP was knocked out only in myeloid cells. The mice exhibited only minimal signs, characterized by a slight slowing of weight gain, compared to the severe physical signs seen in mice in which TTP was knocked out in all cell types.

However, the mice with only myeloid-specific TTP deficiency were highly and abnormally susceptible to a low-dose injection of lipopolysaccharide, or LPS, a major component of the cell wall of Gram-negative bacteria. The low LPS dose given produced no signs in normal mice. However, the mice with TTP deficiency in their myeloid cells rapidly developed signs of severe infection, extensive organ damage, and TNF levels 110 times greater than in the control group.

The scientists concluded that while myeloid cells aren’t the only ones in which TTP plays an important role in fighting infection, the TTP in myeloid cells specifically is critical for fighting off septic shock caused by Gram-negative bacteria such as *E. coli*.

The study appeared in the May issue of the Journal of Immunology.



*Stumpo has co-authored more than 50 papers since 1981, 45 of them with Blackshear. (Photo courtesy of Steve McCaw)*



*Citation: Qiu LQ, Stumpo DJ, Blackshear PJ. 2012. Myeloid-specific tristetraprolin deficiency in mice results in extreme lipopolysaccharide sensitivity in an otherwise minimal phenotype. J Immunol 188(10):5150-5159.*

(Cindy Loose is a contract writer with the NIEHS office in Bethesda, Md.)

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## Genetic stature puzzle leads to interwoven complex traits

*By Carol Kelly*

Understanding why African Pygmies are so short — the average adult male height is 4 feet 11 inches — is a longstanding biological mystery. After investigating this genetic puzzle, Sarah Tishkoff, Ph.D., a professor of genetics and biology at the University of Pennsylvania (UP), suggests that variants leading to short stature could be attached to a genetic code beneficial for adapting to life in a tropical environment.

While no single gene tied to short stature was found in her new [study](#), several genomic regions associated with local adaptation were discovered.

“The adaptive process that produced small body size in Pygmies may be the result of selection for traits other than stature, including early reproduction, metabolism, and immunity,” posits Tishkoff, recipient of an NIH Pioneer Award funded by an NIEHS [grant](#).

### Mining population genomics data

The [Tishkoff Lab](#) specializes in studying genetic variation at the genome level in global populations, but only recently have the tools to uncover complex DNA processes become available. To provide a genome-wide look at the adaptive and genetic basis of short stature in Pygmies, Tishkoff took a multifaceted approach. Her quest was to identify genes responsible for stature determination.

To start the research, Tishkoff and colleagues compared DNA from a group of Pygmies with that of their Bantu neighbors in Cameroon. The Bantu were chosen as the comparison group, because of their geographic proximity, striking height difference, and history of mixed reproduction with the Pygmies. Genomic regions reflecting Pygmy or Bantu ancestry were differentiated. The researchers found that Pygmies with more Bantu lineage tended to be taller, suggesting a genetic root for height.





*Tishkoff, who is average in height, towers over two Pygmy women. (Photo courtesy of Sarah Tishkoff)*



**Linked video:**

[Watch scenes from Africa as Tishkoff discusses human origins in Africa and population history](#)

(Launches in new window)

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Next, the genetic variations unique to Pygmies were explored. The detailed analysis found multiple Pygmy-specific signals of selection in genomic regions, likely tied to local adaptation. On chromosome 3, several genes stood apart from others.

### Linking height and disease susceptibility

One gene in particular, the CISH gene, is known to play a role in both growth hormone response and susceptibility to infectious diseases, such as malaria and tuberculosis. Within the intricate links of genetic code, stature could be tied to immunity and ability to reproduce at a young age among the Pygmy population in Cameroon.



*Bedzan Pygmies in Cameroon (Photo courtesy of Sarah Tishkoff)*

Given that Pygmies have an expected lifespan of only 18 years and typically live in microbe-dense tropical forests, their abilities to reproduce early and fight infection faced strong adaptive selection pressure. If the genetic expressions leading to these beneficial responses are also tied to height, short stature could simply be a byproduct of other adaptive traits.

Everything is interconnected, according to Tishkoff. “One of the major challenges in the post-genomic era is understanding the complex web of genetic, developmental, physiological, and environmental interactions underlying continuous trait variation, including susceptibility to disease,” she was quoted as saying in the [UP announcement](#) of her Pioneer Award.

*Citation:* Jarvis JP, Scheinfeldt LB, Soi S, Lambert C, Omberg L, Ferwerda B, Froment A, Bodo JM, Beggs W, Hoffman G, Mezey J, Tishkoff SA. 2012. Patterns of ancestry, signatures of natural selection, and genetic association with stature in Western African Pygmies. PLoS Genet 8(4):e1002641.

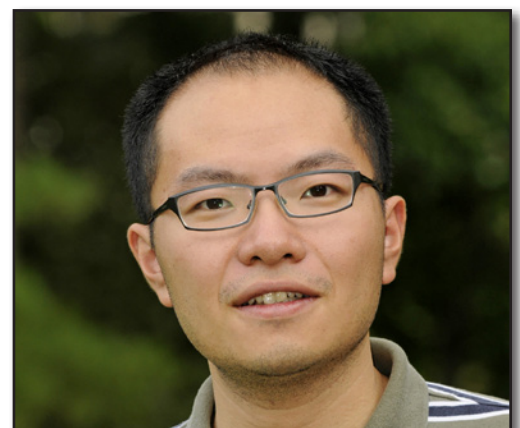
(Carol Kelly is a research and communication specialist with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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## Cell Biology Group fellow wins travel award

*By Eddy Ball*

NIEHS visiting fellow Fumin Lin, Ph.D., has won a \$1,000 travel award for research he presented at the NIH Stem Cell Research Symposium May 10-11 in Bethesda, Md. Fumin, who is a member of the [Cell Biology Group](#) headed by [Anton Jetten, Ph.D.](#), chief of the Laboratory of Respiratory Biology, will be able to use his award to attend a stem cell meeting of his choice.



*Travel award winner Lin joined NIEHS last year to work on the diabetes stem cell project. (Photo courtesy of Steve McCaw)*



The [NIH Center for Regenerative Medicine \(NIH CRM\)](#) and [Stem Cell Interest Group \(SCIG\)](#) co-sponsored the symposium, which highlighted NIH intramural stem cell research projects, with a focus on NIH CRM-funded investigators. Jetten's group is one of three at NIEHS headed by lead researchers who are affiliated faculty with the NIH CRM.

The award-winning research is part of work in the Jetten group on the role of transcriptional regulator Gli-similar (Glis) 1-3 proteins in the generation of pancreatic beta cells, as part of the development of an innovative therapy for the treatment of patients with diabetes, which currently affects approximately 10 percent of the U.S. population.

Lin and Jetten successfully induced differentiation of human adipose-derived stem cells, human embryonic stem cells, and induced pluripotent stem cells into pancreatic endocrine cells. Their results suggest that Glis3 plays an important role in the differentiation of stem cells into beta cells, and upregulating expression of Glis3 might benefit cell replacement therapy against diabetes, offering an alternative treatment to insulin therapy, which does not prevent long-term complications from the disease.

Presentations at the symposium covered embryonic stem cells, induced pluripotent stem cells, and various types of adult stem cells. Additionally, there was a focus on determining the roadblocks to clinical translation of stem cells for cell therapies and screening small molecules.

Keynote speakers were NIH CRM Director [Mahendra Rao, M.D., Ph.D.](#), and SCIG steering committee co-chair [Manfred Boehm, M.D.](#), head of the Laboratory of Cardiovascular Regenerative Medicine at the National Heart, Lung, and Blood Institute.

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## Council talks focus on DNA repair

*By Heather King*

The National Advisory Environmental Health Sciences (NAEHS) Council meeting May 22 at NIEHS featured scientific talks by Massachusetts Institute of Technology professor and Pioneer Award winner [Leona Samson, Ph.D.](#), and head of the NIEHS DNA Replication Fidelity Group [Thomas Kunkel, Ph.D.](#) Both talks addressed the importance of DNA repair in determining the ultimate effects of environmental exposures, from ultraviolet (UV) light to heavy metals, on human health.

The ability to correct mistakes, or lesions, in DNA that would otherwise lead to illness and disease varies greatly among individuals and is referred to as DNA repair capacity. Differences in repair capacity help explain why some individuals are more likely to fall ill from chemical exposures or develop skin cancer from sun damage, while others remain healthy.



*In 2011, Jetten received an award of NIH Common Fund money through the NIH CRM ([see story](#)) to support his group's research. (Photo courtesy of Steve McCaw)*

## Samson's pioneering methods to analyze DNA repair capacity

Samson began her talk, “Developing Novel Methods to Measure DNA Repair Capacity in Humans,” by describing different types of DNA damage and the different biological repair strategies that specifically address them. One of the better-defined repair processes, nucleotide excision repair (NER), is important in correcting DNA damage by ultraviolet (UV) rays and is disrupted in the disease xeroderma pigmentosa (XP). As DNA lesions from UV exposure build up, XP patients acquire numerous skin malignancies from an early age.

Early methods for quantifying DNA repair capacity relied on expressing a reporter gene from a plasmid that contains UV-induced damage that is known to inhibit mRNA transcription. Reporter expression was robust in normal cell lines that can repair the damage, but very poor in XP cell lines that are deficient in repair. The protein produced by the reporter could then be detected based on its activity in enzyme assays, allowing researchers to quantify the amount of repair taking place.

### Going from one channel to five

Using the host cells' ability to reactivate the expression of a reporter gene in a repair-dependent manner is also the basis of Samson's new system for measuring DNA repair capacity, which is capable of tracking multiple DNA repair pathways simultaneously with an easy to read output. Instead of using a single reporter, however, Samson's system uses different shades of fluorescent proteins.

When repair occurs at a plasmid with one type of lesion, a particular shade of light can be emitted by its fluorescent protein. This system allows researchers in her lab to monitor a variety of reporters and repair pathways simultaneously with a simple fluorescent light detector.

Using this system, Samson's group has been able to evaluate DNA repair systems including NER, homologous recombination, mismatch repair, and MGMT direct reversal repair. Samson also spoke of the possibility of using these repair capacity reporting plasmids in cell lines derived from patients, which would allow a person's DNA repair capabilities and deficiencies for specific types of damage to be determined.



*Samson is one of just two NIEHS-funded researchers who have won the coveted Pioneer Award, which is designed to support individual scientists of exceptional creativity who propose pioneering, and possibly transforming, approaches to major challenges in biomedical and behavioral research. (Photo courtesy of Steve McCaw)*

## Fundamental, exposure, and translational research

The study of DNA repair helps scientists understand not only the different types of DNA damage and how they occur in response to various environmental exposures, but also the critical role of damage control in human health. Just as it is sometimes better to ask for forgiveness than permission, sometimes biology finds it more efficient to allow mistakes and correct them as necessary.

Understanding what occurs during various repair processes, how these processes help humans respond to harmful exposures, and how to determine a particular patient's risk for disease based on repair capacity fulfills several NIEHS goals, promising to continue making good returns on the investment NIEHS makes in the critical field of DNA repair research.



## The bigger picture

Samson is now looking forward to using her fluorescent reporter system as a guide to direct more detailed studies of other kinds of DNA damage that do not inhibit transcription. By using high throughput sequencing technology, Samson can see how damage and repair affect transcriptional mutagenesis wherein the damaged DNA template encodes mRNAs with inappropriate sequences that may not make functional proteins.

## Kunkel drives home the challenge of DNA replication fidelity

Kunkel began his talk, “The consequences of DNA replication infidelity in human health,” by drawing the audience in with a metaphor for the impressive biology that lets healthy people avoid replication errors. Imagine, he said, typing 2,000 copies of a lengthy textbook with no mistakes between 8 a.m. and 4 p.m. If that text book were the human genome, the workday would represent the 8 hours of S phase.

Of course, much like a typist, the DNA replication machinery relies on its versions of the backspace function, exonuclease activity, and spellcheck, mismatch repair, as well as hitting the right keys, nucleotide selectivity.

Kunkel went on to explain the importance of the complex interaction between the polymerase making the new DNA strand and each incoming nucleotide that will be added. He showed atomic resolution structures of the new nucleotide snugly fitting into its spot in a polymerase and described the different polymerases important for proper replication.

## TLS polymerases allow infidelity

After describing the scrupulous fidelity of most DNA replication polymerases, Kunkel introduced the translesion synthesis (TLS) polymerases, which are less picky and more flexible in their active sites, allowing them to replicate damaged DNA. This allows TLS polymerases to correct lesions, as they do to prevent the type of UV damage seen in the XP patients also described by Samson. These more liberal polymerases also allow errors when mutagenesis is beneficial, such as during antibody production. In this manner, TLS polymerases make the new DNA more as it should be by allowing it to be less like its template.

## RNA in the DNA

Kunkel also spoke about another type of mistake during replication — the insertion of RNA bases into a new strand of DNA. Ribonucleotides contain an extra oxygen atom that can result in strand cleavage and genome instability, and the incorporation of ribonucleotides leads to damage-susceptible DNA. Why, then, have Kunkel’s group and others observed such a high rate of ribo incorporation where the corresponding DNA nucleotides should be? His research and that of others suggest there may be a signaling function behind ribonucleotide incorporation. Kunkel’s lab is excited about further examining the causes for, and ultimate effects of, ribonucleotide incorporation on human health.

(Heather King, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Structural Biology Protein Expression Core.)



*In 2011, NIH promoted Kunkel to the rank of NIH Distinguished Investigator, one of the highest honors NIH awards to its scientists, and one that only an estimated two to three percent of NIH scientists ever achieve. In addition to leading his research group, Kunkel is also head of the Laboratory of Structural Biology. (Photo courtesy of Steve McCaw)*

# Drastic reduction in air pollution may decrease CVD risk

By Carol Kelly

By identifying the positive health effects of a reduction in air pollution exposure, a new [NIEHS-funded](#) study led by [Junfeng \(Jim\) Zhang, Ph.D.](#), a professor in the Keck School of Medicine at the University of Southern California (USC), shows how air pollution contributes to cardiovascular disease (CVD) risk.

“We believe this is the first major [study](#) to clearly demonstrate that changes in air pollution exposure affect cardiovascular disease mechanisms in healthy young people,” said Zhang.

This environmental health research, with real-world conditions, was possible because the Chinese government agreed to temporarily improve air quality in Beijing, as a stipulation for hosting the 2008 summer Olympic Games. To clean up Beijing for the Olympic Games, factories were closed down and car traffic was limited. This governmental air quality intervention set the stage for a controlled examination of pollution-mediated health effects.

“Beijing is one of the most polluted cities in the world,” said Zhang. “We wanted to take advantage of such a huge intervention and look at what happens to people biologically.”

Seizing the unique opportunity to gauge changes in air quality, a team led by Zhang measured air pollutants before, during, and after the Olympic Games. At the same time, the researchers also measured seven markers of cardiovascular health in 125 healthy, non-smoking, young people, who were an average of 24 years old. Several blood plasma factors, cell counts, blood pressure, and heart rate were examined.

## Air pollution exposure linked to risk for cardiovascular disease

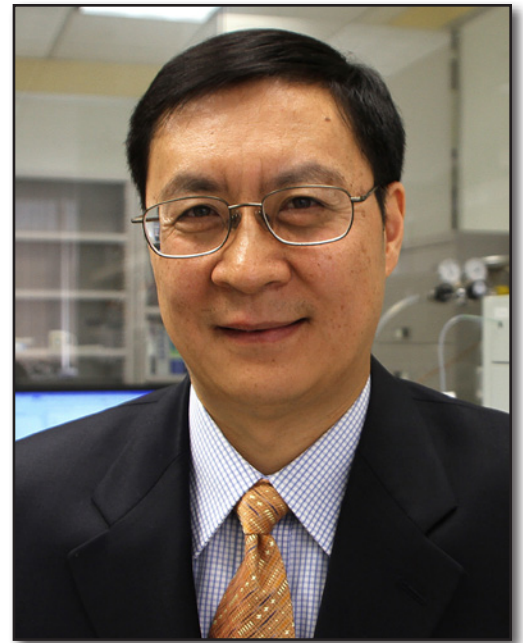
During the Games, air pollutant concentrations decreased substantially. These air quality improvements were associated with improved biological measurements in the young adults, indicating decreased risk for cardiovascular problems. However, when industrial and automotive activity resumed in Beijing, the cardiovascular health indicators returned to high-risk levels.

Thus, the short-term reduction in air pollution levels during the games led to temporary improvement in cardiovascular health among study participants.

Although the research did not quantify the risk from air pollution exposures, it provides invaluable information for improving the assessment of public health impacts of air pollution reduction.

## Public health impacts

During the past two decades, both chronic and short-term air pollution exposures have been related to cardiovascular diseases in numerous observational studies. But few studies have examined how the environment affects disease pathways. Through the investigation of biological indicators clinically related to cardiovascular morbidity or mortality, the work of Zhang’s research team stands apart.



*At USC, Zhang leads large studies to investigate air pollution health effects, using both biochemistry tools and epidemiological approaches. (Photo courtesy of the University of Southern California)*



According to the American Heart Association, air pollution can trigger heart attacks and other heart problems, especially in people with underlying cardiovascular conditions. This new study shows that even healthy people, like the young adult participants, may experience cardiovascular disease symptoms from exposure to elevated levels of air pollution. In the United States, more than 40 percent of people live in areas where air pollution threatens their health, according to the American Lung Association State of the Air 2012 report.

Large numbers of people around the world are exposed to air pollution levels as high as Beijing's, explained Jonathan Samet, M.D., director of the USC Institute for Global Health.

Zhang and fellow authors maintain that their findings further provide data to support the argument that air pollution may be a global risk factor for cardiovascular disease.

*Citation:* Rich DQ, Kipen HM, Huang W, Wang G, Wang Y, Zhu P, Ohman-Strickland P, Hu M, Philipp C, Diehl SR, Lu SE, Tong J, Gong J, Thomas D, Zhu T, Zhang J. 2012. Association between changes in air pollution levels during the Beijing Olympics and biomarkers of inflammation and thrombosis in healthy young adults. JAMA 307(19):2068-2078.

(Carol Kelly is a research and communication specialist with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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## CNS program participants gather at NIEHS

*By Ernie Hood*

The [NIEHS Centers for Neurodegeneration Science \(CNS\)](#) program held its fourth annual meeting May 3-4 at NIEHS, with approximately 65 scientists and trainees from the centers ([see text box](#)) joining scientists and administrators from the Institute.

Established in 2008 to build upon the success of the previous Collaborative Centers for Parkinson's Disease Environmental Research program, the five-year CNS initiative funds integrated basic and clinical research to elucidate the environmental and genetic interactions that contribute to the development of Parkinson's disease (PD) and related neurodegenerative diseases. The highly collaborative, cross-disciplinary work being conducted at the centers, located at Emory University, University of California, Los Angeles (UCLA), and the Sanford-Burnham Medical Research Institute, has spawned new understanding of the role of the environment in the pathogenesis of neurodegenerative diseases, as well as the discovery of important new biomolecular mechanisms, therapeutic targets, and treatment modalities.

The annual meeting gathers center directors, project investigators, trainees, and NIEHS scientists to highlight findings emerging from each center and to provide a forum for discussion of current trends in the field. "It's very important for the centers to get together and



*Kirshner welcomed the CNS investigators to their fourth annual meeting at NIEHS. (Photo courtesy of Steve McCaw)*

update each other on what's going on and what progress has been made in the year," said meeting co-organizer Annette Kirshner, Ph.D., one of the NIEHS scientific program administrators who oversee the CNS program. "It's also a wonderful opportunity to start establishing collaborations between and among centers, and sometimes all three of them have a hand in something."

## Center reports

At the meeting, each of the centers reported on the progress of their research projects since last year's gathering. They all have projects exploring the role of exposures to environmental toxicants, particularly pesticides, such as rotenone, maneb, and paraquat, in the loss of dopaminergic neurons in the brain's substantia nigra region, which leads to PD.

The Emory center, directed by Gary Miller, Ph.D., is working to improve understanding of how environmental toxicants disrupt dopamine homeostasis, mitochondrial function, and redox balance in the substantia nigra, and how the affected neurons respond to such insults. Miller and his colleagues have also developed a mouse model genetically engineered to produce low amounts of VMAT2, a protein used in dopaminergic neurons to clear away excess dopamine. Inhibition of the protein can lead to PD. The team also reported significant progress in the use of high-resolution metabolomics to identify blood biomarkers of PD risk.

At the UCLA center, co-directed by Mary-Francoise Chesselet, M.D., Ph.D., and Beate Ritz, M.D., Ph.D., research on PD and the environment runs a bidirectional gamut, from cell-based experiments through other model organisms such as *Drosophila*, zebrafish, and mice, and into humans, as well. The group has identified an association between exposure to specific pesticides and increased risk of PD, in an exceptionally well-characterized patient cohort in the agricultural region of California's Central Valley. An animal model project has shown that traumatic brain injury causes progressive death in dopaminergic neurons, and when combined with later pesticide exposure, a synergistic effect leads to a substantially greater risk of developing PD. The team confirmed the phenomenon in the Central Valley human cohort.

Researchers at the Sanford-Burnham center, directed by Stuart Lipton, M.D., Ph.D., are studying the effects of environmental stress, represented by oxidation and S-nitrosylation, on PD-related proteins, and are working to develop new therapeutics with high-throughput screening of chemical libraries using platforms of lower organisms such as *Drosophila* and in recombinant and cell-based screens. The hits derived from those assays are then further tested in human embryonic stem cell (hESC)-derived dopaminergic neurons. The hESC model is also being used to study developmental vulnerability to PD-related abnormal proteins or oxidative/nitrosative stress as the stem cells differentiate into dopaminergic neurons.



*NIEHS Division of Extramural Research and Training Director Gwen Collman, Ph.D., updated CNS participants on the progress of the new NIEHS Strategic Plan and the status of the NIH Blueprint for Neuroscience Research. (Photo courtesy of Steve McCaw)*



*NIEHS intramural researchers working on Parkinson's disease also provided updates on their scientific progress to CNS annual meeting attendees. Jau-Shyong Hong, Ph.D., from the Neuropharmacology Group in the Laboratory of Toxicology and Pharmacology, described his group's work on the role of microglial NADPH oxidase in PD pathogenesis. (Photo courtesy of Steve McCaw)*



*Health Scientist Administrator Mike Humble, Ph.D., presented the ins and outs of grantsmanship and training opportunities with NIH. (Photo courtesy of Steve McCaw)*





Poster displays in the lobby outside Rodbell Auditorium afforded CNS investigators the opportunity to present their work. UCLA postdoc Hakeem Lawal, Ph.D., left, described his poster to trainees and scientists from other centers. (Photo courtesy of Steve McCaw)



Sanford-Burnham's Lipton, left, and Emory's Dean Jones, Ph.D., took advantage of the poster session to continue their collaboration, an important component of the CNS program. (Photo courtesy of Steve McCaw)



Sanford-Burnham CNS investigator Rolf Bodmer, Ph.D., left, and Emory CNS Director Miller were among the participants in a panel discussion on the future of PD research and the CNS program that closed out the meeting. (Photo courtesy of Steve McCaw)



UCLA CNS co-director Chesselet, who is also a member of the National Advisory Environmental Health Sciences Council at NIEHS, made several pertinent points during the meeting's closing discussion session about integration of research in human, animal, and cell models. (Photo courtesy of Steve McCaw)

## Training and CNS

In addition to the scientific proceedings, the meeting represented a unique opportunity to enhance training among the centers' members, many of them junior investigators at an early stage in their careers. According to leaders of the initiative, training and career development are indispensable elements of the CNS program, for some very solid reasons.

“What’s happening in science these days is that we’re graying out, and for a variety of reasons it’s not been easy to get the next generation up the ladder to start replacing all of us graying-out people,” said Kirshner. “Also, trainees very often get trained in disciplines that were practically nonexistent when their mentors started out. So trainees are an integral part of the research projects, and that kind of diversity is needed.”

Miller noted that the center model provides a unique forum for effective training. “When you have this sort of center model, you have graduate students and postdocs [with] four or five mentors, because they’re collaborating between those groups,” he said. “So it creates a much richer training environment for them, because they’re exposed to tools and approaches that they otherwise wouldn’t have, and it’s done in an organized fashion. So I think that’s really helped out a lot of our trainees to see this collaborative, interactive nature, which is really the wave of the future in science. And seeing how it works in practice as a trainee is really helpful for that.”

Chesselet cited the long-term professional relationships formed during training and the use of training opportunities to help attract early-stage researchers to the environmental health sciences. “There are two aspects to training. One is the trainees in our labs, and I can tell you from the experience that I had with the previous iteration of these centers, I am still in contact with trainees from that time, who are now young faculty, and I’m still having a mentoring role in development of their careers, because we met when they were young trainees.”

“I hope that the same will happen with the current trainees,” she continued. “In addition, one of the trainees from my lab is now a postdoc in another lab in the consortium, and that it is a continuation for him, but he is also learning a lot of new things. Also, a lot of these young scientists would never have paid attention to environment if they had not been brought in and seen not only what’s done in our lab, but in the center and then among the other centers. If you catch people very early and give them passion for a particular field of science, they are much more likely to stay with it, and that’s really important.”

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison.)

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## Predicting breathing rates with personal exposure monitors

*By Nancy Lamontagne*

New personal monitoring technology, developed by NIEHS grantees, measures exposure levels and predicts breathing rates based on movement. Since a person running or even walking breathes much faster than someone sitting on a bench, this technology could provide a more accurate assessment of how much pollution a person inhales, and help to strengthen associations between environmental exposures and disease.



A pilot [study](#), published in the journal *Atmospheric Environment*, showed that the new technology accurately predicted breathing rates for most of the 22 adult participants wearing personal exposure monitors during a variety of activities.

“The exposure estimates used in past studies may not have represented the amount of pollution that actually entered the body,” said Charles Rodes, Ph.D., senior fellow at RTI International in Research Triangle Park, N.C., and senior author for the study. “The new technology could be useful for understanding how environmental exposures affect asthma and other diseases.”

### Multi-institute collaboration

Researchers from RTI, the Massachusetts Institute of Technology (MIT) in Cambridge, Mass., Columbia University in New York, and Stanford University in California, all contributed to the new technology, through a collaboration funded by a Genes, Environment, and Health Initiative (GEI) Exposure Biology Program grant award. The Exposure Biology Program, a component of GEI, supports researchers developing technologies to measure environmental exposures that contribute to the development of disease.

Rodes explained that RTI and Columbia had incorporated accelerometers that sense movement in three directions into their prototype personal exposure devices to monitor compliance. Meanwhile, researchers led by William Haskell, Ph.D., professor emeritus at Stanford, and Stephen Intille, Ph.D., formerly a professor at MIT and now at Northeastern University, were using a wireless accelerometer and a mobile phone to collect 24-hour activity and sleep information. The researchers from the various institutions met at a GEI meeting and began brainstorming about how to better use accelerometer data.

### Linking breathing and moving

The MIT group developed an algorithm to translate the accelerometer motion information into a sensitive variable to predict breathing rates, and the groups worked together to develop protocols to test the algorithm using the personal exposure devices developed by the RTI and Columbia researchers. The algorithm worked well and showed a linear relationship between the accelerometer data and breathing rate for a variety of activities, such as sitting, standing, and walking, when participants wore the monitors on the hip, ankle, upper arm, thigh, or in the pocket. It did not work as well when the monitor was worn on the arm, the activity was bicycling, or the adults were more than 70 years old.



*RTI's compact MicroPEM device measures particulate matter and incorporates accelerometer technology that allows the prediction of breathing rates. (Photo courtesy of RTI International)*



*Rodes said that the grant award allowed the researchers to greatly extend the value of their work in a timely manner. (Photo courtesy of RTI International)*

Steven Chillrud, Ph.D., a researcher at Columbia and co-author of the study, said that the researchers who collaborated on this work have also collected data on 20 boys and girls, ages 11 to 15, to see if the monitors work equally well in children. Although more studies are needed, the personal monitor could be particularly useful for children, because it is comfortable to wear.

“Next, we have to show that the technology really improves the accuracy of exposure measurements,” Rodes said. NIEHS epidemiologist Matthew Longnecker, M.D., Sc.D., proposed that the team help validate the accuracy of the new technology by using the RTI device to measure 48-hour exposure to indoor air pollution from cookstoves in South Africa.

*Citation:* Rodes CE, Chillrud SN, Haskell WL, Intille SS, Albinali F, Rosenberger M. 2012. Predicting adult pulmonary ventilation volume and wearing compliance by on-board accelerometry during personal level exposure assessments. *Atmospheric Environment*; doi:10.1016/j.atmosenv.2012.03.057 [Online 6 April 2012].

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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## Scientists explore developmental origins of disease

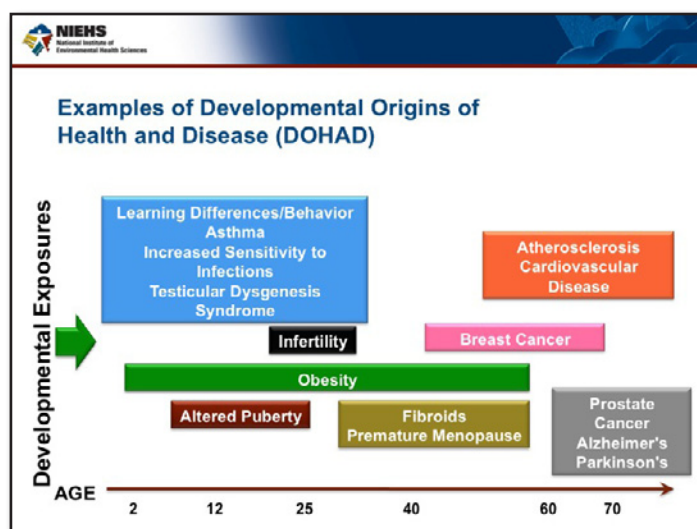
*By Thaddeus Schug*

Experts from around the world gathered May 14-16, at the Espace Saint-Martin Conference Center in Paris, to examine the animal and human data supporting the hypothesis that exposures during fetal and postnatal development can lead to functional deficits and increased disease risk later in life. The meeting was attended by more than 250 participants, many of them leading researchers on early-life exposures and diseases.

The meeting was the [third International Conference on Fetal Programming and Developmental Toxicity \(PPTOX III\)](#), titled “Environmental Stressors in the Developmental Origins of Disease: Evidence and Mechanisms.” Meeting co-chairman Philippe Grandjean, M.D., opened the meeting, stating, “The goal here is to examine the animal and human data that supports the hypothesis.” Grandjean went on to note that scientists participating in the conference would be reporting findings that identify some of the mechanisms for the effects, as well as identify research gaps and challenges.

### Developmental effects of early-life exposures

NIEHS Health Scientist Administrator Jerry Heindel, Ph.D., followed Grandjean with a presentation titled “Developmental Programming by Nutrition or Environmental Chemical Exposures: Two Sides of the



*Birnbaum pointed to some of the age-dependent disease risks associated with early-life environmental exposures. (Slide courtesy of Linda Birnbaum)*



Same Coin.” Heindel argued that the adverse effects caused by poor early-life nutrition are very similar to the effects of chemical exposures during early stages of development. According to Heindel, “Both poor nutrition and environmental exposures are likely occurrences for many populations, and thus a high percentage of individuals may be at risk of environmental-induced diseases.”

Heindel and others referred to work performed by David Barker, M.D., Ph.D., who, in the mid-1980s, found a negative correlation between birth weight and the rate of death from coronary heart disease, later dubbed the **Barker Hypothesis**. The concept that stressors, early in life, influence later-life health outcomes, now includes non-nutritional early-life exposures that have been shown to alter the body’s physiology, and is termed the developmental origins of health and disease hypothesis.

NIEHS/NTP Director Linda Birnbaum, Ph.D., was a very active participant during the meeting, repeatedly questioning, challenging, and offering scientific insight. Birnbaum also delivered a very animated presentation titled “Environmental Stressors in the Development of Disease: Where Do We Go From Here?” Birnbaum noted that developmental toxicity is a particularly difficult field to study. “We must focus our concern on functional deficits now, rather than just investigating known diseases such as cancer,” added Birnbaum, underscoring both the challenges of the research and its tremendous potential for preventing disease.

Robert Barouki, M.D., of Paris Descartes University, co-chair of the conference organizing committee, closed the meeting with a challenge to policymakers to take action to prevent developmental toxicity. Barouki stated, “Scientific evidence is now available, which wasn’t the case a few years ago. Nutritional imbalances or exposure to certain chemicals during the prenatal period could have consequences for health later in life. Although we don’t know the exact magnitude of the consequences, the science is there and is ripe for public action.”

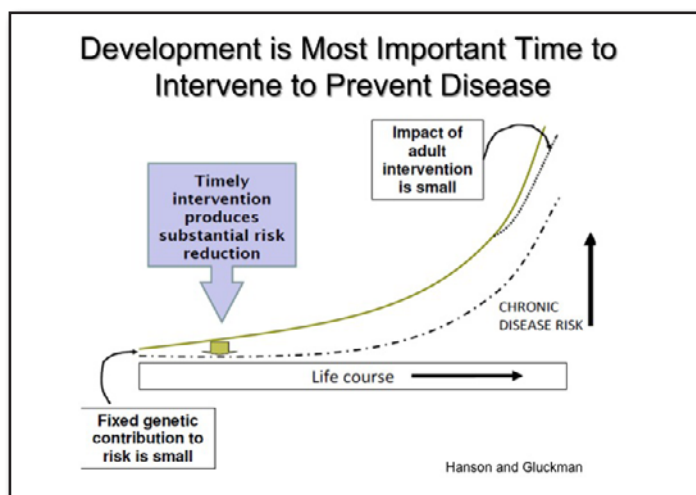
The PPTOX IV meeting will be held Nov. 5-7, 2014, at the International Conference Center in Kitakyushu, Japan.



The three-day meeting was held May 14-16, 2012, at the Espace Saint-Martin Conference Center in Paris. (Photo courtesy of PPTOX)



PPTOX IV will be held Nov. 5-7, 2014, at the International Conference Center in Kitakyushu, Japan. (Photo courtesy of PPTOX)



Heindel emphasized that exposure prevention in early life can have substantial impact on disease prevalence later in life. (Graphic courtesy of Jerry Heindel)

## Preconference symposium on preventing non-communicable diseases by reducing early-life exposures

As part of the Institute's efforts to increase awareness of the role of environmental exposures in global health, NIEHS organized a four-hour symposium May 13 on early-life exposures and opportunities for [primary prevention](#) of non-communicable diseases (NCDs).

The symposium, held in conjunction with the PPTOX III meeting in Paris, brought together international leaders in the global initiatives with leading scientific experts in epigenetics and developmental origins of health and disease, to combat the major NCDs, such as cancer, chronic lung disease, diabetes mellitus, and cardiovascular disease. Organized by NIEHS Senior Advisor for Public Health John Balbus, M.D., and a planning committee that included Heindel, the event featured keynote presentations by Birnbaum and Grandjean, an NIEHS grantee, as well as the head of The NCD Alliance Ann Keeling. A closing panel that included Cristina Rabadan-Diehl, Ph.D., deputy director of the Office of Global Health at National Heart, Lung, and Blood Institute, discussed how this emerging science could be incorporated into ongoing and planned prevention strategies for NCDs.

The symposium involved many of the speakers and organizers for the PPTOX III general meeting. Balbus said that participants plan to submit a commentary from the workshop for publication in *The Lancet*.

(Thaddeus Schug, Ph.D., is a health scientist in the NIEHS Division of Extramural Research and Training (DERT) and a regular contributor to the Environmental Factor.)

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## This month in EHP

*By Eddy Ball*

The striking cover of this month's [Environmental Health Perspectives \(EHP\)](#) sets the stage for a news feature article titled "Our Food: Packaging and Public Health," discussing some of the environmental health pros and cons of common food packaging materials. The article examines potential chemical exposures from the variety of food containers the average person encounters throughout the course of a day.

A second news feature explores the less beneficial implications of communicating technological and biomedical breakthroughs in "One Study, Two Paths: The Challenge of Dual-Use Research." With the potential to harm as well as help human health, so-called dual-use research challenges researchers, funding agencies, and scientific journals to balance academic and scientific freedom against protection of public health.



<http://twitter.com/ehponline>





In this month's [Researcher's Perspective](#) podcast, host Ashley Ahearn discusses the state of the science on low-dose exposures to endocrine disruptors and the implications for safety testing with guest Laura Vandenberg.

Featured commentaries, reviews, and research this month include the following:

- Role of Environmental Chemicals in Diabetes and Obesity
- Which Fish Should I Eat?
- Health Effects of Low-Level Methylmercury
- Malignant Epithelia Transform Normal Stem Cells
- Exposure to Nanoparticles from Cosmetic Powders

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## Upcoming distinguished lecturer Rachel Green

*By Brant Hamel*

The 2011-2012 NIEHS Distinguished Lecture Series will welcome Rachel Green, Ph.D., June 12 at 11:00 a.m. in Rodbell Auditorium, where she will give a talk titled "Quality Control on the Ribosome During Translation." Green's visit is hosted by Traci Hall, Ph.D., lead researcher and head of the [Macromolecular Structure Group](#) at NIEHS.

[Green](#) is a professor of molecular biology and genetics at Johns Hopkins University School of Medicine and a [Howard Hughes Medical Institute Investigator \(HHMI\)](#). She obtained her B.S. from the University of Michigan, a Ph.D. in biological chemistry from Harvard University, and completed her postdoc at the University of California, Santa Cruz.

Author of more than 50 papers, many of them published in high impact journals, Green also serves on editorial boards for the journals RNA, the BMC Journal of Biology, and Molecular Cell. In addition to her HHMI honors, she has won numerous awards, including a Burroughs Wellcome Career Award, a Searle Scholarship Award, and a David and Lucille Packard Fellowship Award. Proving that her commitment to teaching is just as great as her dedication to research, Green was selected as the John Hopkins University School of Medicine Teacher of the Year in 2005. In May, the National Academy of Sciences announced the election of Green as a member, in recognition of her distinguished and continuing achievements in original research.

The Green lab focuses on understanding the mechanism of translation by the ribosome as well as its regulation by extra-ribosomal factors. Her research touches on the RNA world, a concept that the earliest life forms used RNA as both an informational template and as catalytic machinery, prior to the evolution of DNA and protein biochemistry. In fact, during her graduate studies Green was able to engineer an RNA molecule capable of self-replication.



*Green is a synthesizer, both of the disciplines of chemistry and biology, and of the investigations of RNA translation and evolutionary biology.  
(Photo courtesy of Rachel Green)*

During her postdoc, Green became fascinated with understanding how the ribosome exerts such exquisite control over the fidelity of protein synthesis. She employs mutational and enzymological techniques to understand the function and regulation of both prokaryotic and eukaryotic ribosomes. Green's work has important clinical relevance, as many antimicrobials target ribosomal function. Her distinguished lecture will focus on the myriad mechanisms ribosomes utilize to ensure the correct translation of RNA to protein.

*Citation:* Djuranovic S, Nahvi A, Green R. 2012. miRNA-mediated gene silencing by translational repression followed by mRNA deadenylation and decay. *Science* 336(6078):237-240.

(Brant Hamel, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Molecular Endocrinology Group of the Laboratory of Signal Transduction.)

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## Quality control during translation in bacteria and yeast (abstract by Rachel Green, Ph.D.)

Accurate translation of the genetic information is a defining feature of the ribosome and the translation factors. Here we focus on quality control during translation in two different organisms, *E. coli* and *S. cerevisiae*. While much is known about the events that lead to ribosomal discrimination against the incorporation of the wrong amino acid (the process known as tRNA selection), less is known about the ribosomal response following a miscoding event. Using a well-defined *in vitro* bacterial translation system, we identified an unanticipated quality control system on the ribosome that monitors fidelity retrospectively. The *in vitro* and *in vivo* approaches that we have used to define this quality control system will be described. We have also begun to define the biochemical parameters of quality control systems in an *in vitro* reconstituted yeast translation system. In these studies, we have shown that two factors implicated in no-go decay, Dom34 and Hbs1, promote subunit dissociation and peptidyl-tRNA drop-off on the ribosome to initiate the recycling events that eventually lead to mRNA decay. Our most recent work has focused on understanding how the multifunctional ABC-family protein Rli1 contributes to translational termination and recycling. All of these results will be discussed with a view towards defining the relationship (i.e. coupling) between termination and recycling in bacteria and eukaryotes.

## Upcoming workshop on *Leptospira* vaccine potency testing

By Debbie McCarley and Cathy Sprankle

An upcoming workshop will focus on improved methods and approaches for *Leptospira* vaccine potency testing that may also help reduce, refine, and replace animal use. The “International Workshop on Alternative Methods for *Leptospira* Vaccine Potency Testing: State of the Science and the Way Forward” will take place Sept. 19-21 at the U.S. Department of Agriculture (USDA) Center for Veterinary Biologics at the National Centers for Animal Health in Ames, Iowa.

The National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) at NIEHS is organizing the workshop in collaboration with the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and partner organizations in the International Cooperation on Alternative Test Methods. The organizing committee for





the workshop includes scientists from the National Institute of Allergy and Infectious Diseases (NIAID) and the Centers for Disease Control and Prevention, as well as from the USDA and other U.S. and international government agencies.

### **Leptospirosis is a neglected tropical and zoonotic disease**

Leptospirosis is a bacterial zoonotic disease caused by spirochetes of the genus *Leptospira*. More than 500,000 human cases of leptospirosis occur worldwide each year, with a fatality rate of up to 25 percent in some regions. Designated as a neglected tropical disease by the NIH and a neglected zoonotic disease by the World Health Organization, leptospirosis is a global research and public health priority. According to Suman Mukhopadhyay, Ph.D., bacterial zoonoses program officer, NIAID is currently funding several major leptospirosis research grants, which include investigations of mechanisms involved in the infectious cycle, enhanced tools for clinical diagnosis, and target identification for therapeutic intervention and development of potential vaccines for humans.

In the U.S., *Leptospira* vaccines are used in cattle, swine, and dogs to protect them from disease and to reduce the risk of animal-to-human transmission. Human vaccines are also available in some countries outside the U.S. Manufacturers test the potency of vaccine lots prior to their release to ensure their effectiveness. However, methods currently used to test the potency of *Leptospira* vaccines involve large numbers of laboratory animals. Many of these animals experience significant unrelieved pain and distress, with *Leptospira* vaccine testing accounting for over one third of the animals reported to the USDA in this category.

NICEATM and ICCVAM promote the translation of innovative science and technology into improved alternative methods that are more efficient and that can also reduce, refine (enhance animal well-being and lessen or avoid pain and distress), and replace animal use. One of their highest priorities is promoting development and use of improved alternative test methods for vaccine potency and safety testing. NICEATM, ICCVAM, and their international partners recently identified *Leptospira* vaccines as a top priority.

### **About the workshop**

This workshop will bring together international scientific experts from government, industry, and academia to review recent advances in science and technology, in addition to available methods and approaches for *Leptospira* vaccine potency testing. The main focus of the workshop will be on improved methods and approaches and that may provide improved accuracy, efficiency, and worker safety, and that are more humane and use fewer or no animals. Participants will develop a strategy to achieve global acceptance and implementation of scientifically valid alternative methods. A poster session will feature presentations on current research, development, and validation of alternative methods for *Leptospira* vaccine potency testing.

### **For more information**

Registration information and a workshop program will soon be available on the [NICEATM-ICCVAM website](#). NICEATM and ICCVAM also invite the submission of abstracts for scientific posters to be displayed during this workshop. Abstracts should be submitted by August 13.

(Debbie McCarley is a special assistant to Rear Adm. William Stokes, D.V.M., director of NICEATM. Cathy Sprankle is a communications specialist with ILS, Inc., support contractor for NICEATM.)



*The upcoming workshop was an activity recommended by participants at a workshop on alternative methods for vaccine testing organized by NICEATM and ICCVAM in 2010. Members of the ICCVAM Interagency Biologics Working Group pictured here at the 2010 workshop include, back row from left, Juan Arciniega, D.Sc., U.S. Food and Drug Administration (FDA); Marlies Halder, V.M.D., European Union Reference Laboratory for Alternatives to Animal Testing; Janet Skerry, U.S. Department of Defense; Richard Isbrucker, Ph.D., Health Canada; Hajime Kojima, Ph.D., Japanese Center for the Validation of Alternative Methods; Warren Casey, Ph.D., NIEHS; front row from left, Geetha Srinivas, D.V.M., Ph.D., U.S. Department of Agriculture (USDA); Jodie Kulpa-Eddy, D.V.M., USDA; Richard McFarland, M.D., Ph.D., FDA; William Stokes, D.V.M., NIEHS. (Photo courtesy of NICEATM)*

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## Upcoming workshop on informed risk assessment

*By Eddy Ball*

An innovative interagency program continues its 2012 workshop series with an exploration of “[Systems Biology — Informed Risk Assessment](#)” June 14-15 in Washington, D.C.



The workshop, which is part of the National Academies’ Emerging Science for Environmental Health Decisions series, is free and open to the public. Registrations are now being accepted for [attendees](#) and webcast registration will soon be available.



## Emerging considerations in risk assessment

The workshop will focus on changes in the risk assessment landscape driven largely by phenomenal advances in molecular and systems biology, recent reports from the National Research Council, and volumes of new test data arising from the Tox21 and European Registration, Evaluation, Authorisation, and Restriction of Chemical substances (REACH) programs.

These drivers are prompting scientists to look anew at current efforts to advance risk assessment through systems biology data and ask how it can augment, extend, or replace traditional data. The goal for this meeting is to consider these emerging sciences in systems biology as tools to inform risk assessment and decision-making and to identify what key issues must be addressed.

Sponsored by NIEHS, the program holds three workshops per year on the use of new discoveries, tools, and approaches for guiding environmental health decisions. The workshops provide a public venue for communication among government, industry, environmental groups, and the academic community.

The June workshop is the eleventh in the [series](#), which began in July 2009 with a workshop on “Use of Emerging Science and Technologies to Explore Epigenetic Mechanisms Underlying the Developmental Basis for Disease.” Past presentations are archived online, and videos are available for several recent workshops.

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## Extramural papers of the month

*By Nancy Lamontagne*

- [Prenatal exposure to PAHs linked to childhood obesity](#)
- [BPA associated with IVF implantation failure](#)
- [Guidelines for risk of illness from beach sand](#)
- [DNA mismatch repair introduces mutations in non-dividing cells](#)



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

## Prenatal exposure to PAHs linked to childhood obesity

An NIEHS grantee reports that pregnant women exposed to higher concentrations of polycyclic aromatic hydrocarbons (PAHs) were more than twice as likely to have children who were obese by age 7 than women with lower levels of exposure. PAHs are a common urban air pollutant, and this study provides evidence that prenatal exposure to PAHs can influence childhood obesity.

The study involved 702 non-smoking African-American and Hispanic pregnant women, 18-35 years old, living in predominantly low-income areas. A personal air monitor recorded PAH exposure for two days during the mothers' third trimester.

Compared with children of mothers with lower levels of exposure to PAHs during pregnancy, the children of women exposed to high levels were 1.79 times more likely to be obese at age 5 and 2.26 times more likely to be obese at age 7. The 7-year-olds, whose mothers had the highest exposures, had an average of 2.4 pounds of more fat mass than children of mothers with the least exposure.

*Citation:* Rundle A, Hoepner L, Hassoun A, Oberfield S, Freyer G, Holmes D, Reyes M, Quinn J, Camann D, Perera F, Whyatt R. 2012. Association of childhood obesity with maternal exposure to ambient air polycyclic aromatic hydrocarbons during pregnancy. *Am J Epidemiol*; doi:10.1093/aje/kwr455 [Online 13 April 2012].

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## BPA associated with IVF implantation failure

A study funded by NIEHS showed an association between bisphenol A (BPA) urinary concentrations and embryo implantation failure in women undergoing *in vitro* fertilization (IVF). The carefully synchronized hormonal signals and feedback loops involved in an embryo implanting to the uterus make this stage of prenatal development potentially vulnerable to endocrine disruptors such as BPA, which is found in many consumer products.

The researchers measured the urinary BPA levels of 137 women undergoing 180 IVF cycles at the Massachusetts General Hospital Fertility Center. Overall, 75 IVF cycles (42 percent) resulted in implantation failure. The investigators found that implantation failure was almost twice as likely for women with urinary BPA concentrations of 3.80 to 26.48 micrograms per liter than for women with the lowest concentration of less than 1.69 micrograms per liter.

*Citation:* Ehrlich S, Williams PL, Missmer SA, Flaws JA, Berry KF, Calafat AM, Ye X, Petrozza JC, Wright D, Hauser R. 2012. Urinary bisphenol A concentrations and implantation failure among women undergoing *in vitro* fertilization. *Environ Health Perspect*; doi:10.1289/ehp.1104307 [Online 6 April 2012].

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## Guidelines for risk of illness from beach sand

An NIEHS-funded researcher recently published reference levels for the risk of human illness from pathogens in beach sand. There are no U.S. federal guidelines for assessing when pathogens make beach sand unsafe.

The researchers used quantitative microbial risk assessment and Monte Carlo simulations to calculate beach sand pathogen levels corresponding to the 1.9 percent EPA reference risk for marine water, which is equivalent to 19 illnesses per 1000 swimmers. For beach sand, they calculated reference levels of about 10 oocysts per gram of *Cryptosporidium*, about five most probable number (MPN) per gram for enterovirus, and less than 1,000,000 colony forming units per gram for *S. aureus*.

They also measured pathogen levels in sand at a recreational beach in Miami that is affected by nonpoint sources of contamination and found that pathogen levels were lower than the calculated reference levels. The researchers say that more research is needed to evaluate the risk for skin infections associated with exposure to pathogens in beach sand.

*Citation:* Shibata T, Solo-Gabriele HM. 2012. Quantitative microbial risk assessment of human illness from exposure to marine beach sand. *Environ Sci Technol* 46(5):2799-2805.

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# DNA mismatch repair introduces mutations in non-dividing cells

NIEHS grantees report a role for DNA mismatch repair in creating mutations in non-dividing cells. These mutations can lead to cancer or create beneficial new phenotypes.

DNA mismatch repair removes replication errors by removing mismatched nucleotides. It is a strand-specific process, meaning the process removes only nucleotides on the newly replicated strand of DNA. How eukaryotic cells distinguish the strands is not fully understood, but the cells likely lose the ability to distinguish the strands as replication proceeds.

The researchers introduced specific mispairs into the DNA of yeast cells in a way that let them observe the very rare event of non-strand dependent DNA repair. They found that mispairs, not repaired during replication, sometimes underwent mismatch repair later when the cells were no longer dividing. This repair was not strand dependent and sometimes introduced mutations into the DNA sequence that allowed cells to resume growth. In one case, they observed such mutations arising in cells that had been in a non-dividing state for several days.

*Citation:* [Rodriguez GP, Romanova NV, Bao G, Rouf NC, Kow YW, Crouse GF. 2012. Mismatch repair-dependent mutagenesis in nondividing cells. Proc Natl Acad Sci U S A 109\(16\):6153-6158.](#)

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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## Intramural papers of the month

*By Brant Hamel, Sonika Patial, Jeffrey Stumpf, and Sheetal Thakur*

- [Chromatin structure changes during course of glucocorticoid receptor activation](#)
- [Novel assay measures DNA breaks in human cells exposed to tumor inhibitors](#)
- [Mechanism for endocrine disrupting chemicals is dose and cell type specific](#)
- [SIRT1 is a crucial regulator of mammalian metabolic homeostasis](#)

## Chromatin structure changes during course of glucocorticoid receptor activation

A new study from scientists at NIEHS mapped alterations in the chromatin landscape at glucocorticoid receptor (GR) responsive regions during the course of hormone activation. The findings point to a more nuanced view of chromatin structure and its response to physiological stimuli. The GR initially bound an inactive transitional state between fully open and closed, prior to inducing a transition to an open and transcriptionally active structure.

The researchers measured the degree to which chromatin was open at over 50 sites across the genome, using the formaldehyde-assisted isolation of regulatory elements (FAIRE) technique. Prior to receptor activation, all GR-responsive regions had similar FAIRE signals, indicating common chromatin architecture for GR recruitment, which was confirmed across the genome utilizing next generation sequencing. After receptor activation, the FAIRE signal increased dramatically, though the degree of chromatin opening varied between responsive chromatin regions.

The team found significant changes in chromatin structure as far as 1,000 base pairs away from the site of receptor recruitment, indicating that altered chromatin structure can exist across multiple nucleosomes. Chromatin remodeling was dependent on the activity of the switch/sucrose nonfermentable (SWI/SNF) complex because depletion of Brg-1, a component of the complex, led to significant decreases in FAIRE signal in response to hormone. **(BH)**

*Citation:* [Burd CJ, Ward JM, Crusselle-Davis VJ, Kissling GE, Phadke D, Shah RR, Archer TK. 2012. Analysis of chromatin dynamics during glucocorticoid receptor activation. Mol Cell Biol 32\(10\):1805-1817.](#)

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## **Novel assay measures DNA breaks in human cells exposed to tumor inhibitors**

In a recent issue of PNAS, NIEHS scientists report a method to accurately measure the number of DNA breaks that can be induced in human cells. Pioneered by members of the Chromosome Stability Group, they utilized this technique to determine how certain cancer inhibitors modulate DNA break repair.

The study used human cells containing a circular minichromosome from the Epstein-Barr virus. Like any circular DNA, the minichromosome is expected to be supercoiled if there are no breaks. A single-strand break (SSB) relaxes the DNA and a double-strand break (DSB) generates a linear molecule. Lead author Wenjian Ma, Ph.D., exposed cells to ionizing radiation and was able to separate the different configurations of the minichromosome, in order to measure how many molecules contained each type of DNA break and how quickly the DNA was repaired.

The researchers focused on a single class of chemotherapeutic agents that inhibit the poly(ADP-ribose) polymerase (PARP). PARP inhibitors can kill particular types of cancer cells that are defective in DSB repair and recombination processes. The study shows that while reducing PARP protein expression does not affect break repair, some PARP inhibitors impede SSB repair, but not DSB repair. The complexity of chemotherapeutic effects on repairing DNA emphasizes the importance of this novel technique and subsequent findings, in future studies to understand the connections between cancer treatment and DNA repair. **(JS)**

*Citation:* [Ma W, Halweg CJ, Menendez D, Resnick MA. 2012. Differential effects of poly\(ADP-ribose\) polymerase inhibition on DNA break repair in human cells are revealed with Epstein-Barr virus. Proc Natl Acad U S A 109\(17\):6590-6595.](#)

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## Mechanism for endocrine disrupting chemicals is dose and cell type specific

NIEHS researchers have uncovered the mechanisms by which endocrine disrupting chemicals (EDCs) initiate adverse effects on human cells. They found that bisphenol A (BPA) and bisphenol AF (BPAF), two synthetic chemicals found in polycarbonate plastics and electronic materials, and Zearalenone, an estrogenic mycotoxin found in cereal crops and bread, can function as both agonists and antagonist EDCs. Since EDCs are widely present in the environment, this study may help scientists understand the impact of environmental exposure on human health and wildlife populations. Previous experimental studies have shown that the antagonistic effects of BPA at low concentrations inhibit key adipokines, which are thought to protect humans from complex diseases, such as the induction of metabolic syndrome.

Researchers used three different human cell lines with low endogenous expression of estrogen receptor (ER) alpha to assess the estrogenic actions of the three EDCs. The results showed that both BPA and BPAF act as antagonists for ER alpha and ER beta at low concentrations, less than 10 nanomolar, but act as agonists at higher concentrations, greater than 10 nanomolar, in a cell specific manner. The findings may help explain the tissue selective actions. Moreover, these EDCs not only activate endogenous ER alpha target genes, but can also mediate rapid action responses, such as the activation of p44/p42 mitogen-activated protein kinase (MAPK) pathway, which indicates their mechanisms of action may also involve not only gene responses, but also extranuclear cell signaling activities. **(SP)**

*Citation:* Li Y, Burns KA, Arao Y, Luh CJ, Korach KS. 2012. Differential estrogenic actions of endocrine-disrupting chemicals bisphenol A, bisphenol AF, and Zearalenone through estrogen receptor alpha and beta in vitro. *Environ Health Perspect*; doi:10.1289/ehp.1104689 [Online 11 April 2012].

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## SIRT1 is a crucial regulator of mammalian metabolic homeostasis

In a new study from NIEHS, scientists demonstrated that SIRT1, a highly-conserved nicotinamide adenine dinucleotide (NAD<sup>+</sup>)-dependent protein deacetylase, is an essential factor in the regulation of systemic energy and steroid hormone homeostasis. Mice lacking one copy of the SIRT1 gene showed compromised handling of metabolic stress following a high fat diet. Since SIRT1 has been implicated in a variety of metabolic disorders, such as obesity, diabetes, and related inflammatory disorders, this work strengthens the understanding of the role of SIRT1 in metabolic dysfunctions and identifies it as a potential therapeutic target.

Using metabolomic and biochemical tests on a heterozygous SIRT1 mouse model, the scientists showed that these mice were susceptible to metabolic abnormalities, such as obesity and high blood glucose, in response to a high fat diet. Furthermore, SIRT1 insufficient mice demonstrated significant alterations in free fatty acid recycling in the liver and increased testosterone levels. The observed increase was attributed to impaired hepatic inactivation and clearance of testosterone in these mice.

This study further establishes SIRT1 as a crucial modulator of metabolic equilibrium and may help in the development of novel therapeutic interventions that target SIRT1 in metabolic disorders, such as type 2 diabetes and obesity. **(ST)**



*Citation:* [Purushotham A, Xu Q, Li X](#). 2012. Systemic SIRT1 insufficiency results in disruption of energy homeostasis and steroid hormone metabolism upon high-fat-diet feeding. *FASEB J* 26(2):656-667.

(Brant Hamel, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Laboratory of Signal Transduction. Sonika Patial, D.V.M., Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction. Jeffrey Stumpf, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Genetics. Sheetal Thakur, Ph.D., is an IRTA fellow in the NIEHS/NTP Toxicology Branch.)

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# Inside the Institute

## NIEHS health and fitness week becomes a family affair

By Ian Thomas

May 14 marked the beginning of NIEHS' annual Health and Fitness Week, though this year's event brought with it an added twist, by including Family Day as part of the weeklong slate of events. Through a partnership with [Be Active North Carolina](#), a local organization devoted to promoting greater physical activity throughout the state, NIEHS welcomed all comers, young and old, to take part in the educational fun.

"Health and Fitness Week is always great for energizing people around the Institute," said Dona McNeill of the NIEHS Office of Management. "However, our hope is that by weaving Family Day activities into the mix, and allowing people to get involved with their kids, we can foster more conversations at home about things like nutrition and daily exercise."

### The couch potato alternative

Throughout the day, parents and kids took part in a number of events, all designed to help build better habits with regard to nutrition and physical activity. Among them were exercise trivia, a two-mile nature walk, and a scavenger hunt, to name a few.

"Our goal is to promote physical activity and active play, to North Carolinians of all ages, as a means to a healthy lifestyle," said Richard Rairigh, Be Active director of programs and early childhood development. "Be it through partnerships like this one with NIEHS, or others with senior centers, area sports teams, or local schools and child care centers, we'll work with anyone in the community who shares in our vision."

Be Active is a statewide initiative designed to empower North Carolinians to live healthier lives, by educating them on the negative effects of inactivity. The organization also works with grassroots and volunteer groups across the state who share in that mission, while advocating for public programs and policies that support it.

### A family flair for science

Of course, Family Day at NIEHS has never been without its science, and 2012 was no different. Among the activities and workshops geared to teach kids about science were "Flubber and Color Change" with Rachel Frawley of the NIEHS [Toxicology Branch](#); "Allergies and the Family" with Donald Cook, Ph.D., of the [Immunogenetics Group](#); and "DNA Detectives" with Ron Cannon, Ph.D., of the [Intracellular Regulation Group](#).

### Other NIEHS Health and Fitness Week activities and competitions

- "The Biggest Loser" Competition
- 3-on-3 Basketball Round Robin
- Basketball Shootout
- Football Throwing Contest
- Corn Hole Competition
- Table Tennis Tournament



Kids rush to give answers in "Exercise Trivia." (Photo courtesy of Steve McCaw)

“Playing ‘DNA Detectives’ with these kids is always such a thrill for me, because you never know where that could lead in the future,” said Cannon, who conducted the workshop with fellow scientists Diane Spencer and Cindy Innes. “Today, they’re learning about gel electrophoresis, but fifteen years from now, they could be analyzing gels of their own as part of a thesis, and that interest will have started right here with a simple game.”

The day also included a family-style lunch in the NIEHS cafeteria, featuring a kid-friendly menu of spaghetti and meatballs, sandwiches, and barbecue chicken, as well as a full slate of games, ranging from karaoke to a cakewalk.

“Showing people how to live healthier lives strikes at the heart of what NIEHS is all about,” Cannon concluded. “Whether it’s learning how the environment affects our DNA, or the value of taking a break from the TV, these are lessons that everyone can take something away from.”

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)



*With his Zen-like concentration on the ball, a carefully focused Greg Travlos, D.V.M., showed that competition at table tennis, though not quite so physical, could also be very intense in its own way. (Photo courtesy of Steve McCaw)*



*Rairigh gave instruction on daily activities for kids. (Photo courtesy Steve McCaw)*



*Kids took a hands-on approach to science. (Photo courtesy Steve McCaw)*



*Health and Fitness Week also gave employees an opportunity to get physical with some aggressive competition on the court. (Photo courtesy of Steve McCaw)*

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# Earth Day presentation on automotive technology



By Robin Arnette

When automotive expert Richard Cregar asked the audience at the Emerging Automotive Technology seminar who was interested in upgrading their transportation, just about everyone raised their hands. Whether they were interested in keeping their fuel costs low or helping the environment, they came to get the facts about the technologies available in today's vehicles.

The NIEHS Environmental Awareness Advisory Committee (EAAC) hosted a presentation by Cregar May 3 as part of its Earth Day celebration.

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**Linked video:**  
[Watch an NIEHS video about the honor of Earth Day and environmental health \(03:38\)](#)  
(Launches in new window)

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Cregar said his Chevy Volt is a blast to drive. “In addition to being very safe, I have great maneuverability, because the 500 pounds of batteries are distributed along the axis of the vehicle on the floor,” he said. “What more could you ask for in terms of weight distribution and center of gravity?” (Photo courtesy of Wilson Community College)

Cregar is an instructor and department head for Advanced Transportation Technologies at [Wilson Community College](#) in Wilson, N.C. He said that the impetus for much of the interest in automotive technology came from the Obama administration’s mandate that, by 2025, American automakers had to produce a fleet average of 54.5 miles per gallon. In other words, car companies must add up the U.S. Environmental Protection Agency’s rated fuel economy for every car they sell and take the average, and the result must be 54.5 miles per gallon. Cregar rhetorically asked audience members, “Can they do that if they only produce gasoline-powered vehicles?”

Out of the several alternative fuel sources he mentioned ([see text box](#)), he said that electric drives were the most efficient.

## Types of electric drives

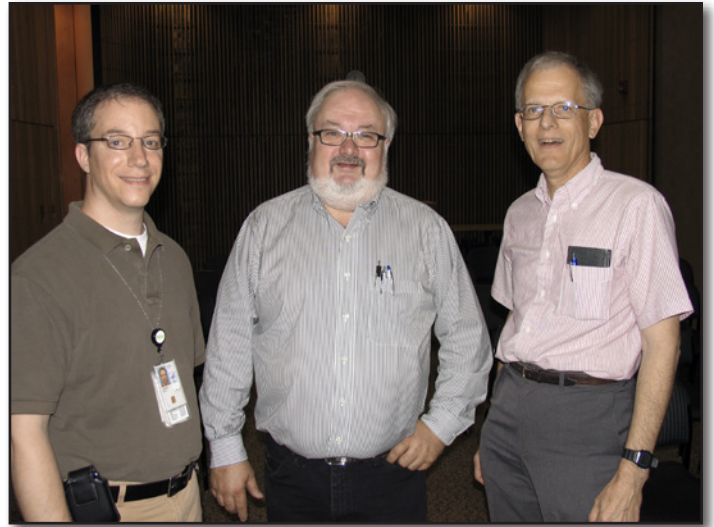
According to Cregar, an example of a mild hybrid system is the eAssist from General Motors. It is currently in the Buick Regal and is the least efficient of the electric drives. A mild hybrid has an electric motor, but it can’t propel the vehicle on its own. It has to work with the internal combustion engine.



In addition to being an advocate for green transportation, Cregar also teaches the next generation of automotive technicians. Within the next five years, he hopes to train enough mechanics to meet the maintenance and repair needs of the growing number of hybrid vehicles. (Photo courtesy of Wilson Community College)

Honda has a medium hybrid system called Integrated Motor Assist (IMA). Medium hybrids differ from mild hybrids by the voltage used and the amount of torque assist available to help propel the vehicle. Medium hybrids also are incorporated into the powertrain, whereas the mild hybrid eAssist is basically a starter/generator that connects to the engine through the serpentine belt drive mechanism.

Cregar said full hybrids are where all the action is in the current market. The Toyota Prius pioneered the genre by producing a plug-in hybrid that has a large electric motor powerful enough to propel the vehicle on its own up to 35-40 mph. After that point, the gas engine switches on, seamlessly, to push the vehicle through increasing wind resistance. General Motors has provided some competition through its Chevy Volt, an extended-range electric vehicle (EREV). An EREV is driven nearly all the time, and at all speeds, by an even more powerful electric motor.



*EAAC coordinators, Paul Johnson, left, and Richard Sloane, right, asked Cregar more questions after the lecture. (Photo courtesy of Robin Arnette)*

## Gasoline isn't the only game in town

Cregar discussed the pros and cons of several other automotive fuel sources during his seminar.

- **Flex Fuel** is 85 percent ethanol and 15 percent gasoline. About 1,600 stations sell flex fuel for the 8 million flex vehicles that are currently on U.S. roads. Although flex owners save 10-12 percent in fuel costs, the vehicles still release carbon into the atmosphere.
- **Biodiesel** offers a clean fuel alternative, but Cregar says its low quantities and chemical instability hinders it from becoming a major player in vehicular drive systems. He said, "Petroleum has been around for a long time, so it's done doing what it has to do to itself. Since biofuels are new, they're still changing, in the pump and in the tank."
- **Clean Diesel** vehicles are a viable option, because they get good mileage and can also use biodiesel fuel. A light-duty, clean diesel truck will have a fuel economy in the low 20s as opposed to the 12 miles per gallon of a regular gasoline pickup. Since clean diesel is still a fossil fuel, these vehicles emit greenhouse gases.
- **Hydrogen** vehicles are clean and only emit water out of their tailpipes. However, hydrogen is the lightest substance in the universe and, as such, poses challenges when it comes to capturing and storing it in large quantities. Cregar rejected hydrogen as an impracticable energy source by saying, "Hydrogen is the fuel of the future and always will be."
- **Compressed Natural Gas (CNG)**, or methane, is a clean energy source mostly used in trucking and heavy equipment. CNG comes from the process known as hydraulic fracturing, or fracking, and has a good long-term price forecast, because of increased domestic production. Nonetheless, CNG vehicles warm the environment, because methane contains carbon.

## Practicing what he preaches

Even though he considers himself a diesel man, Cregar is the proud owner of a Chevy Volt. The Volt uses a lithium battery and is 92 percent efficient when it comes to its fuel consumption. Cregar received countless questions about his car, but one that was on many people's minds was whether or not Cregar would be able to use his car if his family had to evacuate at a moment's notice.

"With the exception of the Nissan Leaf, which is totally electric, all plug-ins, like the Volt, still use gas," he said. "If you have gas in the gas tank, you can go to California right now just like you could in any other car."

Dick Sloane, an EAAC coordinator, has known Cregar for several years and shares his passion for alternative transportation. Sloane knew Cregar was the right choice for this year's Earth Day seminar. "We've gone to a lot of meetings together where he was the featured presenter," Sloane said. "He always presented detailed engineering and scientific facts, not hype."

Cregar stressed that oil will never go away, but it will be much more expensive in the future, because it will be harder to get and cost more to refine. He urges everyone to consider investing in transportation methods that don't depend solely on gasoline. For more information, contact Cregar at [rcregar@wilsoncc.edu](mailto:rcregar@wilsoncc.edu).

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## Labs break for annual strawberry tradition

*By Jeffrey Stumpf*

On a warm, sunny Tuesday afternoon, NIEHS scientists in the Laboratory of Molecular Genetics (LMG) and Laboratory of Structural Biology (LSB) took a break from research to attend the 27th annual strawberry feast May 1, sponsored by the Replication Fidelity Group. Keeping with tradition, the group harvested the strawberries from a local patch in preparation for one of its best-attended events.

LSB chief Tom Kunkel, Ph.D., began the celebration, in front of a capacity audience in the cramped patio on the second floor of the F module in Building 101. The veteran scientist and strawberry festival emcee gave some playful, if unsolicited, fashion advice, suggesting, "Perhaps next year, we'll require a dress code for the strawberry feast — that everybody wear red."



LSB lead researcher Samuel Wilson, M.D., left, and Kunkel, right, show their appreciation for the help of cafeteria manager Lakisha Register. (Photo courtesy of Steve McCaw)

## A bounty of fruit

The epicenter of the feast was a large table with an impressive amount of strawberries, over a dozen cakes, several tubs of ice cream, and many cans of whipped cream. As the crowd encircled the massive dessert display, comments by folks looking forward to their impending indulgence drowned out sporadic mutterings about calorie counting.



Scientist Mercedes Arana, Ph.D., noted that picking strawberries this year proved to be challenging because of the weather and scheduling conflicts. “It had rained recently and was very muddy,” Arana remembered. “Then we realized that we had scheduled a group seminar for a prospective postdoc and had to finish quickly.”

Despite less than ideal conditions, the lab members and their families approached a record for the harvest by gathering about 135 pounds of strawberries.

### A family affair

The tradition started 27 years ago when Kunkel picked enough strawberries for his lab to enjoy. The idea blossomed into a full-fledged festival, attracting hungry scientists in search of a cure for spring fever. For scientist Scott Lujan, Ph.D., the feast has become a family tradition. “My older son has been to the strawberry feast five times, and he just turned four,” Lujan noted. Young Lujan was three weeks old at his first strawberry feast but was unavailable for comment at the time.

Watching the children grow up builds camaraderie and contributes to the family atmosphere of the event and the two departments, which is important to Kunkel. “Strawberries, cake and ice cream make my colleagues smile,” Kunkel said. “They bring their kids too, giving me an excuse to play with them.”



Staff Scientists Jason Williams, Ph.D., left, and Lalith Perera, Ph.D., enjoy the warm afternoon and at least one course of strawberries. (Photo courtesy of Steve McCaw)



The dessert table at the 27th annual strawberry feast attracted employees from across the Institute. (Photo courtesy of Steve McCaw)



Modeling red-only dress codes for future strawberry feasts, postdoctoral trainee Anders Clausen, Ph.D., and fellow strawberry picker Emma Clausen enjoy the fruits of their labor. (Photo courtesy of Steve McCaw)

# Tom's 27th Anniversary Berry Picking! 135 lbs - April 30<sup>th</sup> 2012



*Members of the Replication Fidelity Group and their families braved the elements for the love of strawberries. Pictured from left are Maryam Clausen, carrying Emma Clausen; Clausen; Jessica Williams, Ph.D., with Owen Williams; Lujan, with Logan Lujan; Nan Lujan, Ed.D., with Connor Lujan; Shirley Kunkel; Scott Williams, Ph.D., with Sarah Williams; Danielle Watt, Ph.D.; Frank Boellman, Ph.D.; Kasia Bebenek, Ph.D.; Arana; and Sasha Liberti, Ph.D. (Photo courtesy of Frank Boellman)*

(Jeffrey Stumpf, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group and a regular contributor to the Environmental Factor. He is also a volunteer strawberry tasting consultant.)

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